Potentially Inappropriate Medication use in elderly in a tertiary care centre in South India

An observational study

A dissertation submitted in partial fulfilment of the rules and regulations for M.D branch XVI - Geriatric Medicine examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai, to be held in April 2015

DECLARATION

This is to declare that this dissertation titled

"Potentially Inappropriate Medication use in elderly in a tertiary care centre in South India- an observational study"

Is an original work done by me and submitted in partial fulfilment of rules and regulations for M.D branch XVI Geriatric Medicine examination of the TamilNadu Dr.M.G.R Medical University, Chennai to be held in April 2015.

CANDIDATE

Dr.Alwin Thilak Christopher.J

Post graduate registrar

Dept.of Geriatric Medicine

Christian Medical College

CERTIFICATE

This is to certify that the dissertation entitled, "Potentially Inappropriate Medication use in elderly in a tertiary care centre in South India- an observational study" is a bonafide work

Dr.Alwin Thilak Christopher.J

towards the M.D branch XVI - Geriatric Medicine examination of the TamilNadu Dr.M.G.R Medical University, to be conducted in

April 2015.

GUIDE AND HEAD OF THE DEPARTMENT

Dr.Prasad Mathews

Professor and Head

Dept. of Geriatric Medicine

Christian Medical College

Vellore

PRINCIPAL

Dr.Alfred Job Daniel

Professor

Dept.of Orthopaedics

Christian Medical College

Vellore

CO – GUIDES

Dr.Surekha Viggeswarrpu (Professor, Geriatric Medicine)

Dr.Benny Paul Wilson (Assistant Professor, Geriatric Medicine)

Ms.Mahasampath Gowri (Dept. of Biostatistics)

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LIST OF ABBREVIATIONS AND ACRONYMS

ADR - Adverse Drug Reactions

ADE - Adverse Drug Events

AGS - American Geriatrics Society

Cr Cl - Creatinine clearance

GFR – Glomerular Filtration Rate

GP – General Practitioners

K/DOQI - Kidney Disease Outcomes Quality Initiative

OTC - Over the Counter

PIM – Potentially Inappropriate Medication

1. AIM OF THE STUDY

The aim of the study was to estimate the prevalence of inappropriate medication use in hospitalized elderly over 60 years of age, as defined by the latest updated Beers´ criteria 2012 and to assess the risk factors associated with the use of potentially inappropriate medication.

2. OBJECTIVES OF THE STUDY

1. To study the comorbidity status of the study population
2. To estimate the prevalence of potentially inappropriate medication (individual drug or drug class) use in elderly (more than 60 years of age) hospitalized patients, as defined by the latest updated Beers´ criteria 2012.
3. To assess the risk factors associated with the use of potentially inappropriate medication.
4. To study the use of nephrotoxic drugs and renally inappropriate dosing in the elderly.
5. To estimate the prevalence of polypharmacy and excessive polypharmacy in hospitalized elderly.
6. To study the adverse drug reactions associated with inappropriate drug usage.

3. INTRODUCTION

The world is experiencing a major demographic transition. As a consequence, in developed countries 10% or more of the population are sixty five years of age or over. The situation is moving in the same direction in developing countries like India. Therefore, it is very important to address the health of the elderly. Elderly patients commonly have multiple medical problems requiring treatment. Prescription of medicines plays an important role in the care of elderly people. But unfortunately, many inappropriate drugs continue to be prescribed and used as first-line treatment in older adults. Inappropriate prescribing is considered a major public health issue, given its direct association with substantial morbidity, mortality and health service costs that result from adverse drug reactions (ADRs). Avoiding the use of inappropriate drugs is a simple strategy in reducing medication-related problems in older adults.

Beer's criterion is a well-established method for evaluating appropriateness of drug prescribing in the elderly. It lists a set of drugs which should be avoided in the elderly or used with careful monitoring. This increases the physician's awareness in prescribing medications in the elderly, who are prone to age and disease related decline in physiological reserve. Thoughtful application of the Beers´ criteria will result in better patient outcomes.

Geriatrics is an emerging clinical field in India. Information about the appropriateness of medication use among the elderly in India is limited. Hence, it is necessary to study the appropriateness of prescriptions in our elderly population. Our study focuses on the prevalence and predictors for the use of inappropriate medications in hospitalized elderly patients.

4. LITERATURE REVIEW

4.1 Elderly population – World Demography

The world is experiencing a major demographic transition. As a consequence, in developed countries 10% or more of the population are 60 years of age or over(1). Globally the elderly population is growing at a rate of 2.6% per year. The elderly population is expected to double to around two billion by year 2050 by when there will be more elderly than children. By the year 2050 it is predicted that the number and proportion of the > 80 years age group ("old old") will grow significantly.

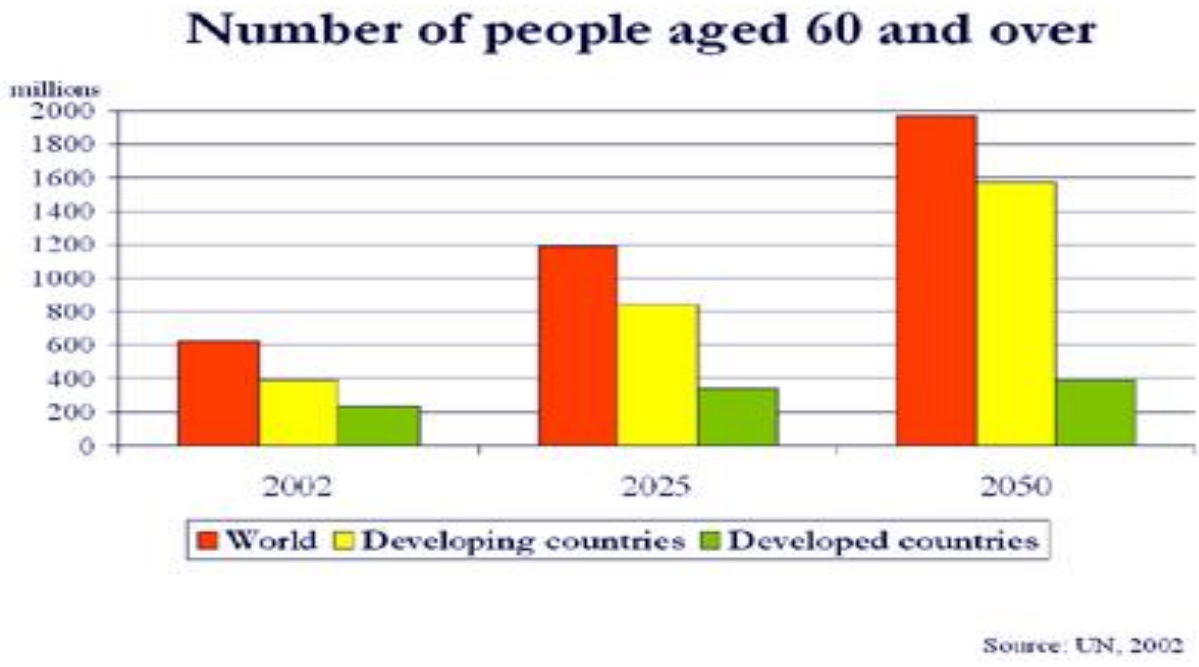

Figure 1 Distribution of elderly in the world(2)

4.2 In India

This demographic trend is similar even in developing countries like India. In India the proportion of the elderly in the total population is rising steadily. The proportion of people >60 years of age was 7% in 2009, and 8% in 2011(3) and it is estimated to rise to 20% in 2050 (figure 2). The absolute elderly population was 88 million in 2009 and is expected to rise to 135 million in 2050(2). More developed states such as Punjab, Himachal Pradesh, and Maharashtra along with Southern states have a higher proportion of senior citizens as compared to other parts of the country.

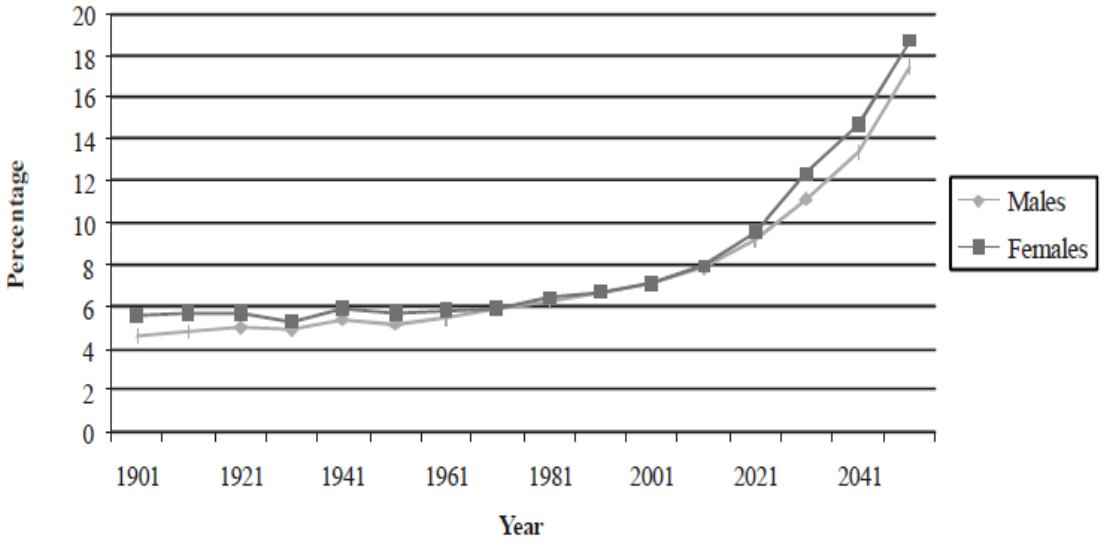

Figure 2 Percentage of elderly (60 and above) by sex, 1901-2051

4.3 Health of the Elderly

Accompanying this demographic shift, it is very important to address the health of the elderly. Elderly patients are extremely vulnerable people and often have multiple medical illnesses which require treatment. Prescribing medicines is a fundamental component in the care of elderly people. It is estimated that medication use among older persons has grown

significantly over the last few decades. About one third of medications are prescribed for patients more than 65 years of age(4), and about three fourths of the elderly population are taking at least one prescribed or non-prescribed drug (US population based study, 2008)(5). Hence there is a potential for increased inappropriate drug prescriptions in the elderly.

4.4 The use of Medications

Medication use is a part of routine living for many individuals. Medications are used in all age groups and the amount of usage is directly proportional to the age and morbidity of the individual. The usage of medications seems to be different in different socio economic classes and genders as well. Although the majority of medications consumed are prescribed medications, other classes such as over-the-counter (OTC) drugs and nutritional supplements, belong to the common pool of drugs consumed(6)(7)(8).

Among the developed nations the percentage of the total national health budget spent on drugs varies between 10 to 20%(9).In developing nations, the medication share of the health budget is between 20 and 40% .

4.5 Definition of Potentially Inappropriate Medication (PIM):

A potentially inappropriate medication is "a drug with which the risk of an adverse event outweighs its clinical benefit, particularly when there is a safer or more effective alternative therapy for the same condition" (10). In general, medicines are considered appropriate when they have a clear evidence-based indication, are safe and well tolerated in the majority and are cost-effective. Inappropriate prescribing also includes inappropriate dose or duration, drug-drug and drug-disease interactions, drug /therapeutic duplication and drug omission. Inappropriate prescribing can be identified using explicit (criterion-based) or implicit

judgement-based) prescribing indicators. Beers´ criteria is the most widely used explicit tool in the literature.

4.6 PIM– A new non communicable disease

Inappropriate prescribing in the elderly is considered a major public health issue, given its direct association with substantial morbidity, mortality and health service costs that result from adverse drug reactions (ADRs). The prevalence of inappropriate medication usage varies between different studies and is dependent on multiple factors. Lusiele et al, in their systematic review and meta-analysis of all the published studies till 2010 have found the prevalence ranging from 11.5% to 62.5 %(11). Indian data shows that about 12 - 20% of elderly community residents are exposed to at least one PIM(12).

PIM usage is associated with an increased risk of adverse drug reactions and hospitalization in the elderly. It accounts for 5 to 23 per cent of hospitalizations, 2 per cent of ambulatory visits and one in 1000 deaths(13) . The Food and Drug Administration has estimated that the cost of hospitalizations due to inappropriate prescription drug use averages $20 billion annually(14).

It had also found that 22- 30% of Adverse Drug Events (ADEs) were preventable by avoiding inappropriate drugs prescribed to the elderly(15). Avoiding the use of inappropriate and high-risk drugs is an important, simple, and effective strategy in reducing medication-related problems and ADEs in older adults.

4.7 Beer´s criteria

Beers´ criterion is an explicit tool to identify inappropriate drug use in elderly population. It is the most widely used tool in research. The following are the merits of Beers´ criteria.

1. It is a well-established and validated tool

2. It remains clinically applicable to both community and residential living elderly.

3. It is updated regularly (latest was published in 2012)

4. A number of observational studies have shown a strong link between the medications listed in the Beers´ Criteria and poor patient outcomes (e.g., ADEs, hospitalisation, and mortality).

Limitations:

It does not address drug omission, drug-drug /drug disease interactions or drug class duplication

4.7.1 Historical aspects of Beers´ criteria

The late Mark Beers´, MD, a geriatrician, developed the set of explicit criteria to assess inappropriateness of drugs prescribed for nursing home residents in 1991 with the help of a team of experts using modified Delphi method. The initial list consisted of a list of 30 drugs to be avoided in the elderly irrespective of the diagnoses. Subsequently Beers´ updated the original criteria by adding new drugs in 1997 and 2003. In 2012, the American Geriatric Society along with a panel of experts updated this list(10).This partnership allows for good wider clinical input and regular systematic transparent updates. This update has much more strength because it grades the strength and quality of evidence of each PIM statement based on level of evidence.

Fifty-three medications are included in the final updated criteria, which were divided into three categories: (Annexure 1)

1. Potentially inappropriate medications to be avoided in older adults, irrespective of diagnosis.

2. Potentially inappropriate medications to be avoided in older adults with certain diseases and syndromes.
3. Medications to be used with caution in older adults

4.7.2 Validation of Beers´ criteria

Shah et al(16) studied the appropriateness of prescribing using Beers´ criteria in 400 patients and they found that drug prescriptions in 291 (72.75%) patients were appropriate and 109 (27.25%) were inappropriate. A total of 2924 formulations were prescribed, of which 2788 (95.34%) were prescribed appropriately and 136 (4.65%) were prescribed inappropriately(17).

In another cross sectional study by Karandikar(18) et al, 600 patients were studied and Beers´ criteria identified 7.3% of potentially inappropriate prescriptions. It is well validated in studies to predict adverse health outcomes due to inappropriate prescribing(19).

4.8 Adverse Drug Reactions (ADR)

Many medications may result in an adverse drug reaction (ADR), defined as "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function".

ADRs are classified as mild, moderate, severe or lethal. ADR can also be classified into six different types; “dose-related (Augmented, also known as “Type A”), non-dose-related (Bizarre, also known as “Type B”), dose-related and time-related (Chronic), time-related (Delayed), withdrawal (End of use), and failure of therapy (Failure)."

4.8.1 Risk factors for Adverse Drug Events

1. Age – pharmacokinetic and dynamic changes
2. Drug factors – polypharmacy, drug duplication, drug–drug /drug –disease interactions
3. Comorbid index
4. Cognition and dependency status
5. Socio - economic factors

4.9 Aging physiology

One thing we learnt in pharmacology in our MBBS days is that "Children are not little adults" and "seniors are not older adults." With aging there is impairment in the regulatory mechanism that maintains the functional integrity of cells, leading to deranged homeostasis under conditions of stress. Important pharmacokinetic and pharmacodynamics changes occur with age. There is a reduction in renal and hepatic clearance. There is an increase in the volume of distribution of lipophilic drugs (hence increasing the elimination half-life of a drug). There is increased susceptibility to side effects of many classes of drugs, especially anticoagulants, vasopressors and psychotropic drugs.

4.10 Polypharmacy

Out of all these risk factors, polypharmacy was found to be the single most significant and independent risk factor in PIM usage and many studies reiterated this fact(20)(21).

Defining polypharmacy continues to be controversial. Polypharmacy can be defined as the concurrent use of many different drugs. Majority of studies have applied five or more drugs as the standard for polypharmacy(22)(23)and defined the usage of 10 or more drugs as excessive polypharmacy. Polypharmacy can also be defined as the use of a number of drugs

in excess of that which is clinically indicated, or the use of an excessive number of inappropriate drugs.

A population-based survey done in the United States showed that more than half of the elderly population use five or more medications a week and 12% use ten or more medications a week(24).

4.10.1 Factors contributing to polypharmacy

Use of multiple drugs is unavoidable in the elderly. The main determinant of polypharmacy is the number of co morbidities. Managing multiple co morbid conditions in old people will be an increasing challenge for medical professionals. The need to keep the number of drugs as low as possible while avoiding under-treatment of the elderly with multiple co morbidities is a difficult balancing act.

Other reasons identified for polypharmacy are,

1. Non-prescription drugs, i.e. Over the Counter (OTC) drugs.
2. Multiple physicians treating one patient.
3. Recent hospitalisation and lack of communication between doctors.

A community survey shows that among the elderly with chronic illnesses as many as 42% used at least one non-medically prescribed drug(25). In the Western literature, vitamins and minerals are the most commonly used (up to 35% of patients) non-prescription drugs. In India, the commonly used non-prescription drugs are - NSAIDs 55%, Antacids 40%, cough expectorants 22% and multivitamin and native medicines contribute 15% each(26) .

Multiple medical professionals treating the patient is the current trend, and it has not spared even a developing nation like India. This is because of the ever increasing number of

specialities and medico legal issues. This can significantly increase polypharmacy because of the communication gap between doctors which is more prominent if the patient had recently been admitted. Hospitalisation is a period where many changes are made to medications.

Australian studies found that, about five to seven changes are made during admission, which includes the stoppage of two to three drugs and the initiation of three to four new drugs. Following discharge, these changes are not communicated to the GPs or the GPs fail to recognise these changes. This can lead on to other problems like drug duplication and drug-drug interactions.

4.10.2 Consequences of Polypharmacy

Besides increasing direct drug costs, polypharmacy increases the risk for adverse drug reactions. The risk of ADRs is found to be 13% with two drugs, 58% with five drugs and 82% with seven drugs(27).

The main reasons for this increased risk of ADR with polypharmacy is the multiple comorbid conditions along with the changes due to normal aging, which increase the drug – drug / drug – disease interactions.

4.11 Drug-drug interactions

The elderly are at high risk for drug interactions due to polypharmacy, co morbidities, and the changes associated with normal aging. The risk of a drug–drug interaction increases with the number of drugs used –in 13% of patients taking two drugs and 82% of patients taking more than six drugs (28). The other main risk factor is using drugs with narrow therapeutic indices like digoxin, warfarin, phenytoin and theophylline.

Other patient conditions associated with excessive polypharmacy include declining cognitive status, poor functional and performance status, poor nutritional status and frailty.

4.12 Drugs and the Kidney

Renal impairment is more commonly seen with the elderly, but unfortunately, the prevalence of older people using renally inappropriate drugs is also on the rise. Both drugs which are directly nephrotoxic drug such as NSAID, ACEI, etc. and drugs which are primarily excreted via the kidney which require dose adjustment are considered renally inappropriate. In a study done by Jones and Bhandari(27) in the United Kingdom more than half the number of the elderly population admitted were prescribed at least one potentially inappropriate medication.

As one grows old, there is a decline in renal function. The main reason is a physiological loss of nephrons as a part of aging, and presence of underlying chronic medical conditions like diabetes mellitus or hypertension which affect kidney function. With a decline in renal function, the drug metabolism, mainly the drug elimination is affected. Drugs which are primarily excreted via the kidney are not cleared promptly in renal insufficiency, and this can lead on to drug toxicity if given at the usual dose. Consequently, dosage of these drugs needs to be adjusted according to the creatinine clearance.

The common marker used to assess the renal functional status is serum creatinine. In the elderly, because of reduced muscle bulk, varied creatinine production and age related decline in glomerular filtration rate, going by creatinine alone will not be reliable, and often even a normal serum creatinine value may not represent normal kidney function. So it is very important to calculate estimated creatinine clearance (Crcl) or Glomerular Filtration Rate (GFR) to know the exact renal function. The K/DOQI clinical practice guideline uses the traditional Cockcroft-Gault equation or the Modification of Diet in Renal Disease (MDRD) study equation (full or abbreviated) for routine estimation of GFR. However studies showed that in patients with a GFR less than 60 mL per minute per 1.73 m2 and in the elderly, the MDRD equation is superior to the Cockcroft-Gault equation(29). Using MDRD equation also

has another advantage of not using weight as a measure; thereby it can predict the exact GFR in obese individuals and in patients with anasarca.

Using renally inappropriate drugs in patients with renal insufficiency can cause drug toxicity and increase the risk of developing ADRs. One-third of total ADRs were related to impaired renal function and most of these ADRs were preventable by omitting the drug altogether or adjusting its dose according to the renal function(30). Therefore, renally inappropriate drugs should be avoided in elderly with renal impairment.

5. METHODOLOGY

5.1 SAMPLE AND SETTING

The study was conducted between April 2013 and August 2014 at Christian Medical College, Vellore, a large tertiary care hospital in South India. Patients greater or equal to 60 years of age, admitted under Geriatric Medicine who fulfilled the inclusion criteria and were willing to participate in the study were recruited into the study. The study and the research procedures were fully explained to the participants and only those who gave written consent /informed consent were allowed to participate in the study. Consent was obtained in the regional language that the patient/relative was conversant with (Annexure 9)

5.2 STUDY DESIGN

This is a prospective observational study done in geriatric patients to assess the prevalence and predictors of inappropriate drug usage and polypharmacy.

5.3 SAMPLE SIZE

The sample size was calculated using an estimated prevalence of inappropriate medication usage as 22% with a 5 % precision using the formula 4pq /d2. This was found to be 275.

5.4 PARTICIPANTS

Inclusion criteria:

1) Patients more than 60 years of age

2) Either the patient or the informant will be able to give a proper drug history

3) Willingness to participate in the study

Exclusion criteria:

All patients who were unable to communicate (i.e., patients on ventilator, seriously ill patients requiring Intensive care unit admissions), patients with poor cognition (with no reliable care giver) were excluded from the study.

5.5 MEASUREMENTS – DATA COLLECTION

The data collection was done in data abstraction forms (Annexure 3) by the principal investigator of the study during the first visit at the time of admission.

The following details were recorded specifically:

1)Demographic parameters – Age, sex, geographic location, occupation, marital and living status, educational level , socioeconomic status as assessed by Modified Kuppuswamy socio economic scale (Annexure 4)

2) Performance status

- Dependency status with Barthel index – 20 point scale (Annexure 5)
- Functional status – walking pattern questionnaire & timed get up and go test (Annexure 6)
- Exertional capacity using NYHA classification
- Cognitive and mood status

3) Comorbidities status assessment – By clinical interview and Charlson comorbidity index

4) Pharmacokinetic parameters – height, weight, BMI, albumin, creatinine including creatinine clearance (both Cockgroft equation & abbreviated MDRD equation) and liver function tests.

5) Details of drug including treatment details and details regarding drug related hospitalisations

Note :

A) Timed get up and go test: Measures mobility in people who are able to walk on their own (assistive device permitted). The person may wear their usual footwear and can use any assistive device they normally use.

1. Have the person sit in the chair with their back to the chair and their arms resting on the arm rests.

2. Ask the person to stand up from a standard chair and walk a distance of 3 ft. (1m).

3. Have the person turn around, walk back to the chair and sit down again.

Timing begins when the person starts to rise from the chair and ends when he or she returns to the chair and sits down. The person should be given 1 practice trial and then 3 actual trials. The times from the three actual trials are averaged.

Predictive Results Seconds Rating:

- <10 sec Freely mobile
- <20 sec Mostly independent
- 20-29 sec Variable mobility
- >30 sec Impaired mobility

B) Walking pattern: The pattern of individuals walking was observed and classified as follows.

- Walks without aid
- Walks with minimal aid, by themselves

- Walks only with major help, and cannot walk themselves
- Not walking and fully bed bound

C) Exertional capacity: The exertional capacity of the individual was classified using the NYHA classification.

- NYHA class 1
- NYHA class 2
- NYHA class 3
- NYHA class 4

Current functioning status was derived by combining the walking pattern, timed get up and go test with effort tolerance classification. This was further divided into three classes:

- Fully functional
- Impaired
- Non functional

D) Cognitive status was assessed using the mini cog screening tool (Annexure 7)

E) Mood status was assessed using the GDS 5 - item questionnaire (Annexure 8)

F) Visual and hearing ability – This was done by assessing the ability of the patient to count fingers at 3 meters, and the ability to hear normal voices from 3 meter distance

5.6 DETAILS OF DRUG USAGE

The details of drugs the patients were currently on (over the previous 2 weeks) were noted in detail.

1) Treatment appropriateness was assessed using the Beers´ criteria (Annexure 1)

2) Essential drug omission was assessed using START criteria (Annexure 2)
3) Drugs with anticholinergic activity in addition to Beers´ criteria were assessed with the criteria studied by Chew et al(31) .
4) Renally inappropriate drugs were assessed in addition to Beer s criteria with the criteria used by Hanlon et al(32)

6. OUTCOMES

6.1 PRIMARY OUTCOMES

1. To estimate the prevalence of inappropriate medication usage in elderly hospitalized patients.
2. To study the comorbidity pattern of the study population
3. To estimate the prevalence of polypharmacy and excessive polypharmacy in hospitalized elderly patients.
4. To estimate renally inappropriate drug usage in elderly hospitalized patient using Beers´ criteria and using Chew et al(31), review article.
5. To estimate the incidence of adverse drug reactions associated with inappropriate drug usage in elderly hospitalized patients

6.2 SECONDARY OUTCOMES:

1. To study the risk factors associated with the usage of potentially inappropriate medication (PIM).
2. To assess the relationship between PIM use and adverse drug reactions (ADRs) in the hospitalized elderly.
3. To assess the relationship between renal impairment and adverse drug reactions (ADRs) in the hospitalized elderly.
4. To estimate the prevalence of drug omission using START criteria.
5. To study inappropriate drug / therapeutic duplication in our study population.

6.3 DEFINITION OF OUTCOME MEASURES

- The prevalence of potentially inappropriate medication usage is defined as the proportion of elderly (more than 60 years of age) who received at least one inappropriate medication (individual drug or drug class), as defined by the latest updated Beers´ criteria 2012, for at least a four weeks continuously.

- Polypharmacy is defined as the concurrent use of five or more drugs and excessive polypharmacy is defined as the concurrent use of 10 or more drugs.

- Renally inappropriate drugs are drugs / class of drugs which are nephrotoxic or drugs or class of drugs which need dose adjustments but are not appropriately adjusted according to the patient's GFR.

- Class 1 PIM (potentially inappropriate medications) are drugs to be avoided in any elderly irrespective of any underlying diseases

- Class 2 PIM are drugs to be avoided in specific disease condition to avoid harmful drug – disease interactions

- Class 3 PIM are drugs which has to be used cautiously in elderly

7. DATA ANALYSIS AND STATISTICAL METHODS

Data entry was done by the principal investigator in the data form and subsequently transferred to Epidata worksheet (Annexure 4). The results were analysed using SPSS software version 22 and stata. The following variables were assessed:

QUALITATIVE VARIABLES	QUANTITATIVE VARIABLES
Living status	Age
Socio economic status	Barthel index
Dependency and functional status	Minicog and GDS
Cognitive and mood status	Co morbidity index
Co morbidity status	Body Mass Index
Treatment characteristics	Creatinine clearance
	Creatinine
	Number of drugs
	Number of PIM
	Number of RIM

Data was analysed using the Student t test, chi square test or Mann Whitney U test and Fisher's exact test based on the normality of distribution of the variables.

Univariate analysis was done to identify the factors which might be associated with inappropriate medication use, adverse drug events and polypharmacy. The factors identified that showed an association with p value less than 0.2 were included in the multivariate analysis and the logistic regression models was done, to measure the statistical significance.

8. RESULTS

8.1 Demographic characteristics

A total of 280 patients, more than 60 years of age, admitted in the geriatric ward, from April 2013 to August 2014, were recruited in the study. The mean age of the study population was around 70.2± 7.5 years with the highest age noted being 96years. The majority of subjects, (72.5%) were 60 to 70 years of age and only 2.9% were above 80 years of age. The distribution of age is summarised in the histogram below (Figure 3). 59.6% (167) of the population were male and 40.4% (113) were female. There was no variation in distribution of age among males and females. About 41.7% were from Tamil Nadu, and the rest were from different regions of India.

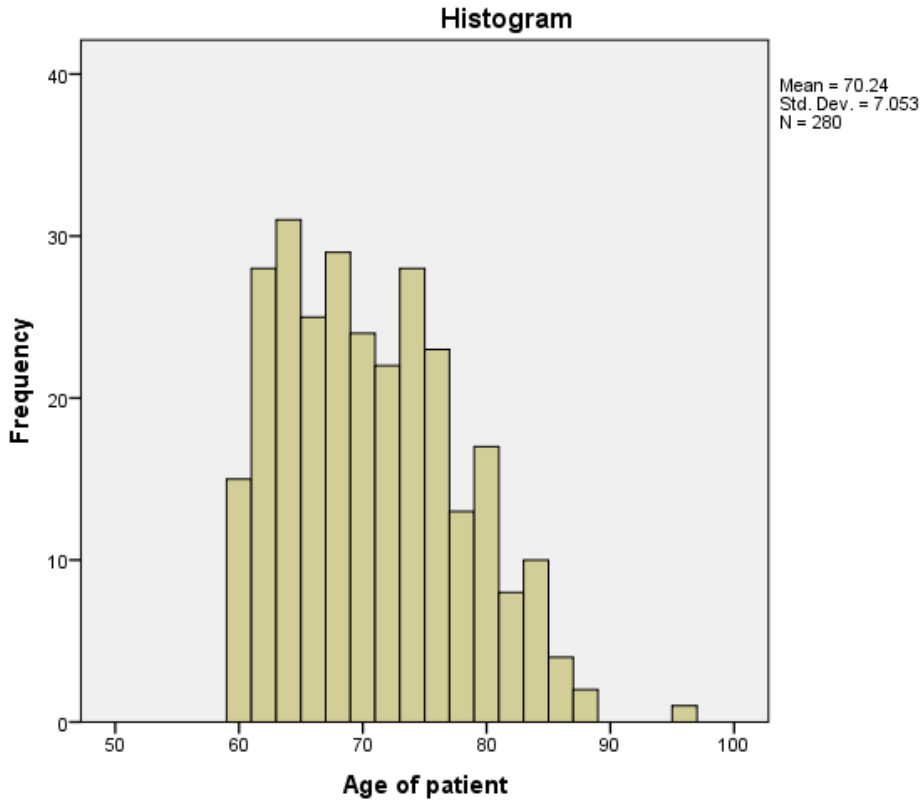

Figure 3 Distribution of age in the study population

8.2 Socioeconomic status

a) The majority of the population (about 97%) were married. About 95.4% lived with either their spouse or children, and only very few, (less than 5%) lived alone or with an informal care giver. Interestingly, out of 9 patients living alone, 8 were females (p 0.003, Pearson chi square test) and 6 patients were more than 75 years of age. (p 0.031, Pearson chi square)

b) About 35.4 % (99) were illiterate. Out of 99 people who were not educated, females comprised the majority with 62.6% (p=< 0.001, Pearson chi square). About 21.1% of people were still working, and others were either retired or not working. Out of people working, males comprised about 87.9 % (p=< 0.001, Pearson chi square).

c) The majority of the population was well above the low socioeconomic status as defined in the last updated Kuppusamy scale (Annexure 4). The majority of the population was middle class, comprising about 62.5%, followed by upper class people (29.3%) and only 8.2% of population belonged to the lower class. Only 17.9% (50) of the population had access to any one of the health related financial support systems. The details of socioeconomic status are listed below in table 1.

Table 1 Baseline demographic characteristics of study population

Baseline demographic characteristics	Counts	Percentage
Mean age is 70.2 ± 7.05 years (60 – 96 yrs.)	280	100
Age distribution		
• 60 to 70 yrs.	203	72.5
• 71 to 80 yrs.	69	24.6
• Above 80 yrs.	8	2.9
Gender		
• Male	167	59.6
• Female	113	40.4
Region		
• In Vellore	91	32.5
• Other parts of Tamil Nadu	26	9.3
• Andhra Pradesh	26	9.3
• North India	109	38.9
• Rest of India	28	10
Marital status		
• Yes	277	98.9
• No	3	1.1
Living status		
• With spouse	158	56.4
• With children	109	38.9
• With informal care giver	4	1.4
• Alone	9	3.2
Educational status		
• Educated	181	64.6
• Illiterate	99	35.4
Level of education		
• Primary schooling	26	9.3
• Secondary schooling	45	16.1
• Diploma	98	35
• Master graduates	12	4.3
Working status		
• Current workers	59	21.1
• Retired	118	42.1
• Not working	103	36.8
Level of work		
• Unskilled	36	12.9
• Semiskilled	26	9.3
• skilled	125	44.6
Medical benefits		
• yes	50	17.9
• no	230	82.1
Economic status (kuppusamy scale)		
• upper class	82	29.3
• upper middle class	72	25.7
• lower middle class	103	36.8
• upper lower class	18	6.4
• lower class	5	1.8

8.3 PERFORMANCE STATUS

a) About 43.2% of people were dependent either partially or completely with no gender, age or class difference. Dependence was further classified objectively with the help of the Barthel index. The results were summarised in table 3.

b) Functional status of an individual was assessed in 2 parts, assessing mobility and the other exertional capacity. Mobility was assessed subjectively with mobility pattern questionnaire and objectively by timed get up and go test and exertional capacity was assessed by NYHA class. Finally the patient's functional status was assessed as functional, impaired or non-functional. Functional patients were those who took less than 10 sec to walk 3 foot distance without support and with an exertional capacity of better than NYHA class 2. Non-functional patients were identified as those who could not walk and remained mostly or completely bed bound with the exertional capacity of NYHA class 3 or 4. The remaining patients were grouped as impaired functional status. The results are summarised in the table below.

c) About 16 %(45) of the population had cognitive impairment affecting their ADLs which was assessed with the help of mini Cog. There was no gender variation in the distribution but there was a significantly higher proportion of dementia with advancing age (p=0.003, Pearson Chi-Square test).

d) Single item questionnaire was used to screen for depression, subsequently followed by 5 item GDS (geriatric depression scale) in our study population. About 17.5% (49) were depressed with no gender difference and the distribution was proportionate across all age groups.

e) About 59 patients in our study had significant insomnia which warranted the usage of sedatives, at some point in their life. There was no gender variation and the distribution was similar across all age groups with no variation in the distribution of insomnia.

f) Almost all the patients (98%), except 6 patients, in our study group had good visual acuity which was assessed by finger counting at 3meters. Out of these 6 people with severe visual impairment, 1 had congenital blindness, 2 had proliferative diabetic retinopathy and the other 3 patients had mature cataract. About 90% of people had cataract (either immature or mature), but only 35.7% of people had undergone cataract surgeries with IOL placement.

g) About 77.1 %(216) of people could hear normal voices at 3 meter distance, and the rest 22.9 %(64) were hard of hearing. Out of 64 people who had hearing impairment, only one patient was using a hearing aid.

Table 2 Performance status of the study population

Performance status assessment	Numbers	Percentage
1. Dependency status		
a) Fully independent for ADLs	159	56.8
b) Partially dependent with Barthel index > 10/20	74	26.4
c) Partially dependent with Barthel index < 10/20	23	8.2
d) Completely dependent for ADLs	24	8.6
2. **Functional status**		
a) **Timed getup and go test**		
• takes less than 10 sec	42	15
• takes 10 – 30 sec	133	47.5
• takes 30 - 60 sec	38	13.6
• takes > 1min	10	3.6
• could not walk	57	20.6
b) **Walking pattern**		
• Walks without aid	148	52.9
• Walks with minimal aid, by themselves	60	21.4
• Walks only with major help , and cannot themselves	39	13.9
	33	11.8

• Not walking and fully bed bound		
c) **Exertional capacity**		
• NYHA class 1	80	28.6
• NYHA class 2	132	47.1
• NYHA class 3	55	19.6
• NYHA class 4	13	4.6
d) Current functioning status		
• Fully functional	32	11.4
• Impaired	215	76.8
• Non functional	33	11.8
3. Cognitive status		
• Normal cognition	237	84.6
• Impaired cognition with Minicog > 1	26	9.3
• Impaired cognition with Minicog ≤ 1	17	6.1
4. Mood status – depression		
• Normal mood / no depression	231	82.5
• Depression with GDS ≤ 3	13	4.6
• Depression with GDS > 3	36	12.9
5. Sleep pattern		
• Normal sleep	221	78.9
• Insomnia	59	21.1
6. Visual ability		
• normal vision (as assessed by finger counting at 3 m)	274	97.9
• vision impaired	6	2.1
• presence of cataract	250	89.5
• presence of IOL in cataract	70	25
7. Hearing status		
• Normal hearing (able to hear 30 db sound)	216	77.5
• Impaired	64	22.1
• Using hearing aid	1	0.004

8.4 COMORBIDITY STATUS

8.4.1 Diabetes mellitus

- A total of 156 people (55.7%) out of 280 patients had diabetes. The mean duration of Diabetes mellitus (DM) in years was 12.1 yrs. ± 8.7yrs, and it ranged from newly diagnosed to as long as 43 years.
- Out of these 156 people with DM, 135 (86.5%) had evidence of diabetic neuropathy. The predominant form (more than 90%) seen was distal sensorimotor polyneuropathy.
- About 50 patients (32%) had laboratory evidence of diabetic nephropathy.
- Out of these 50 patients, 25 patients had evidence of chronic kidney disease (CKD) with crcl < 60. Of these, two were in stage 5 CKD (one required maintenance haemodialysis), 11 in stage 4 and the other 12 in stage 3 CKD.
- 23 patients had diabetic retinopathy, out of which 2 patients had significant vision impairment and had difficulty to even count fingers at 3 meter distance.
- Out of 156 patients, 50 were taking insulin with or without concomitant use of oral hypoglycaemic agents (OHAs), and there were 8 admissions for hypoglycaemia in this group.
- By chi square subgroup analysis there was no difference in occurrence of these hypoglycaemic episodes between diabetics with and without CKD and there was also no age related difference.
- Only 2 people reported hyperglycaemic complications.
- By subgroup analysis with chi square equations, we found that the prevalence of diabetes was more in females, and the occurrence of micro vascular complications, especially nephropathy (p=0.31) and retinopathy (p=0.27) was seen more in males when compared to females, though not statistically significant.

Table 3 Statistics of diabetes mellitus in study population

Patients with diabetes mellitus	156 (55.7%)	124 (44.3%)
With neuropathy	135 (48.2%)	145 (51.8%)
With nephropathy	50 (17.9%)	230 (82.1%)
With CKD	25 (7.1%)	255 (91.1%)
With retinopathy	23 (8.2%)	257 (91.8%)

8.4.2 Systemic hypertension

- This was the most commonly occurring comorbidity in our study population, seen in 222 patients out of 280 (79.3%). Mean duration was 10 years ± 6 years.
- 53 patients (23.9%) had left ventricular hypertrophy (LVH).
- Out of these 53 patients with LVH, 33 patients had diastolic dysfunction. Out of these 33 patients 15 patients had grade 1 diastolic dysfunction, 7 patients had grade 2 diastolic dysfunction, and the remaining 11 patients did not have any echocardiogram done to know the status of diastolic dysfunction.
- 3 patients had evidence of hypertensive nephrosclerosis, and all of them 3 had CKD (2 patients in stage 4 CKD, and 1 in stage 5 non oliguric CKD).
- Out of these 3 patients, 1 had a hypertensive emergency which eventually led onto recent hospitalisation.
- 3 patients had evidence of hypertensive retinopathy, out of which 2 patients had grade 2 HTN retinopathy and 1 had grade 1 HTN retinopathy

Table 4 Statistics of systemic hypertension in study population

Patients with hypertension	222 (79.3%)	58 (20.7%)
With nephrosclerosis	3 (1.1%)	277 (98.9%)
With CKD	3 (1.1%)	277 (98.9%)
With retinopathy	3 (1.1%)	277 (98.9%)
With LVH	53 (18.9%)	227(81.1%)
With diastolic dysfunction	33 (11.8%)	247 (88.2%)

8.4.3 Dyslipidemia

- About 178 patients (63.6%) had dyslipidemia.
- Out of 178, 40 people (22.5%) had fatty liver, 7(4%) had NASH, 2 patients (1.1%) had evidence of Chronic Liver disease (CLD) (one with no evidence of Portal Hypertension (PHT) and decompensation, but the other patient had decompensated chronic liver disease.

8.4.4 Obesity related ailments

- People with obesity (BMI > 30) comprised 39 patients out of 280. 37 had dyslipidemia (almost 95%).
- The mean BMI in people having dyslipidemia was 26 ± 5, which was in the overweight category.
- A greater proportion of males were obese in our study in comparison with females. (p 0.005 in chi square test).
- Of these 39 obese individuals, 29 had obesity sleep apnea (OSA) syndrome. Of these 29, 12 cases were proven by sleep study, but the other 17 were assumed to have probable OSA based on the STOP BANG questionnaire.
- Of these 12 proven cases of OSAS, only 3 were using CPAP.
- Of these 37 patients, 36 had hypertension, 28 had diabetes and 10 had coronary artery disease (CAD).In our study, the disease incidence of DM, HTN and CAD was 55%,79% and 20% respectively, but in these obese individuals, the incidence of DM, HTN & CAD was found to be 97%,75% and 27%,respectively. This is definitely more, again confirming the association of visceral obesity with metabolic syndrome.

Table 5 Statistics of dyslipidemia in study population

Patients with dyslipidemia	178 (63.6%)	102 (36.4%)
With fatty liver	40 (14.3%)	240 (85.7%)
With NASH	7 (2.5%)	273 (97.5%)
With CLD	2 (0.7%)	278 (99.3%)
With obesity	37 (13.2%)	243 (86.8%)
With OSAS	29 (10.4%)	251 (89.6%)

8.4.5 Coronary artery disease

- We had 56 patients (20%) with coronary artery disease. In this group of people, 37 had definite history of acute coronary syndrome (ACS), 5 had angina symptoms, and 1 underwent elective percutaneous transluminal coronary angioplasty (PTCA) . The other 13 did not have any definite evidence of CAD, but were receiving antiplatelets, statins and some even beta blockers.
- Of these 37 people who had a history of ACS, 6 underwent coronary artery bypass grafting(CABG), 6 underwent stenting, 1 was thrombolysed with streptokinase, and the remaining 24 were treated with conventional medical drugs and had not undergone any form of revascularisation surgically or medically.
- Of these 56 patients, 31 had ischaemic cardiomyopathy with systolic dysfunction. The mean ejection fraction (EF) in these patients was 43%± 7 %. Out of 31 with left ventricular (LV) systolic failure, 13 patients had mild LV systolic dysfunction, 3 had moderate LV systolic dysfunction, 4 had severe LV systolic dysfunction, and the remaining 11 patients did not have an ECHO documentation to stage the failure.
- Of these 7 patients with moderate to severe LV systolic dysfunction, 5 patients had been vaccinated with pneumococcal vaccine within the last 5 years. There was no variation with gender or different age classes in the occurrence of CAD and ACS.

Table 6 Statistics of coronary artery disease in study population

Patients with coronary artery disease	56 (20%)	224 (80%)
With History of ACS	37 (13.2%)	243(86.8%)
With LV systolic failure	31(11.1%)	249(88.9%)
With History of revascularisation (stent / CABG)	12(4.3%)	268 (95.7%)

8.4.6 Other causes of cardiac failure

- We had a significant number of patients having cardiac failure secondary to causes other than ischemia.
- Diastolic failure was the most common cause for cardiac failure, occurring in 56 patients (20%), followed by high output failure secondary to anaemia in 7 patients (2.5%), restrictive cardiomyopathy in 3 patients (1.1%), and one patient (0.4%) with dilated cardiomyopathy secondary to alcohol.

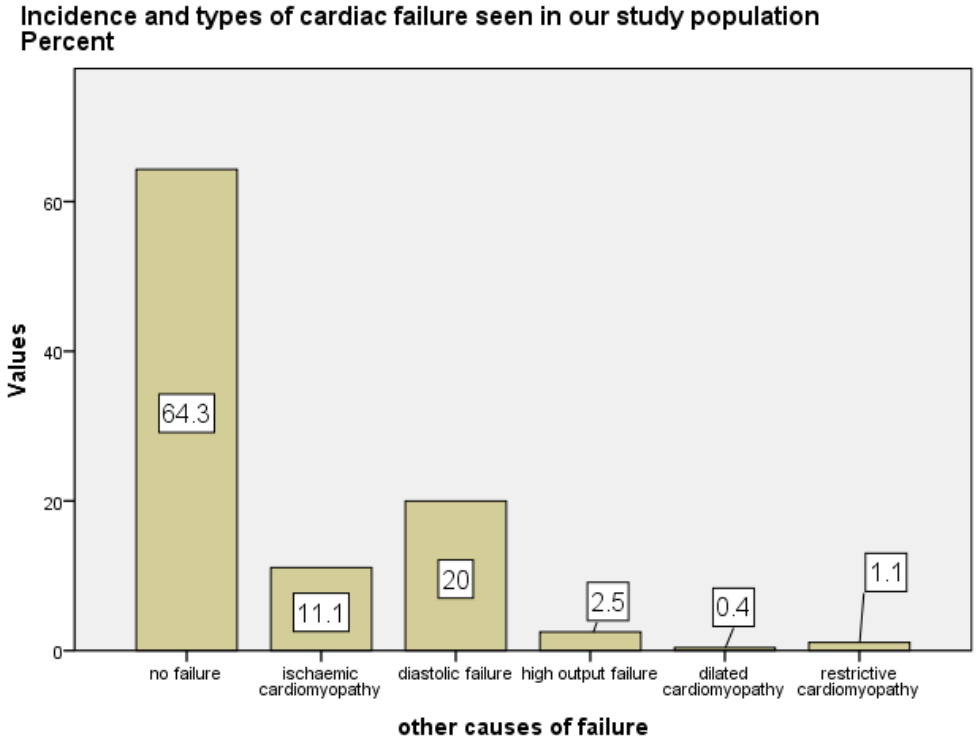

Figure 4 Incidence and types of cardiac failure in study population

8.4.7 Rhythm disturbances:

- Twenty eight patients had rhythm abnormalities, which included 14 cases (50%) of atrial fibrillation, 2 cases (7.1%) of ventricular tachyarrhythmia (1 non sustained ventricular tachycardia, and one of ventricular fibrillation and subsequent cardiac arrest), 2 cases (7.1%) of sinus nodal dysfunction, 5 cases (17.9%) of conduction system disease and other miscellaneous causes in 5 patients (17.9%).
- Out of 28 patients, only one patient had suffered an episode of cardiac arrest which reverted with CPR and was managed medically with amiodarone.
- Both the patients with sinus nodal disease were not on permanent pacemakers. But, one patient with recurrent episode of cardiogenic syncope secondary to atrial tachyarrhythmia underwent permanent pacing.

8.4.8 Cerebrovascular accident

- Forty four patients (15%) had a history of cerebrovascular accident out of which ischaemic stroke dominated with 77.3% (34 cases), haemorrhagic in 13.6% (6 patients), both types in 1 patient and in 4 cases, the nature of stroke could not be identified because of loss of documentation.
- No patient in our study group had undergone any revascularisation procedure (medical or endovascular).
- 8 patients in our study group had suffered recurrent CVAs, out of which 2 were on anticoagulation (1 for cardio embolic stroke secondary to atrial fibrillation (AF), and the other for large artery occlusion)

8.4.9 Chronic obstructive pulmonary disease (COPD)

- Totally 73 patients had airway disease, which comprised 66 patients with COPD and 7 patients with bronchial asthma.

- Out of these 66 patients with COPD, 47 had spirometry reports. The mean FEV1 in patients with COPD was 56% ± 19% of the predicted value. Significant reversibility was seen in 19 patients (40.4%).
- Majority of the COPD patients belonged to GOLD stage 1 and 2, and only 1/4th of population belonged to stage 3 and 4 COPD. The COPD stage distribution across the population is described in Figure 5.
- No patient with severe COPD had any evidence of pulmonary arterial hypertension or right heart failure.
- Out of 73 patients, 41 (56.2%) were using inhalers, either rota halers or metered dose inhalers (MDIs), and 25 (34.2%) patients had been vaccinated with pneumococcal vaccine previously.

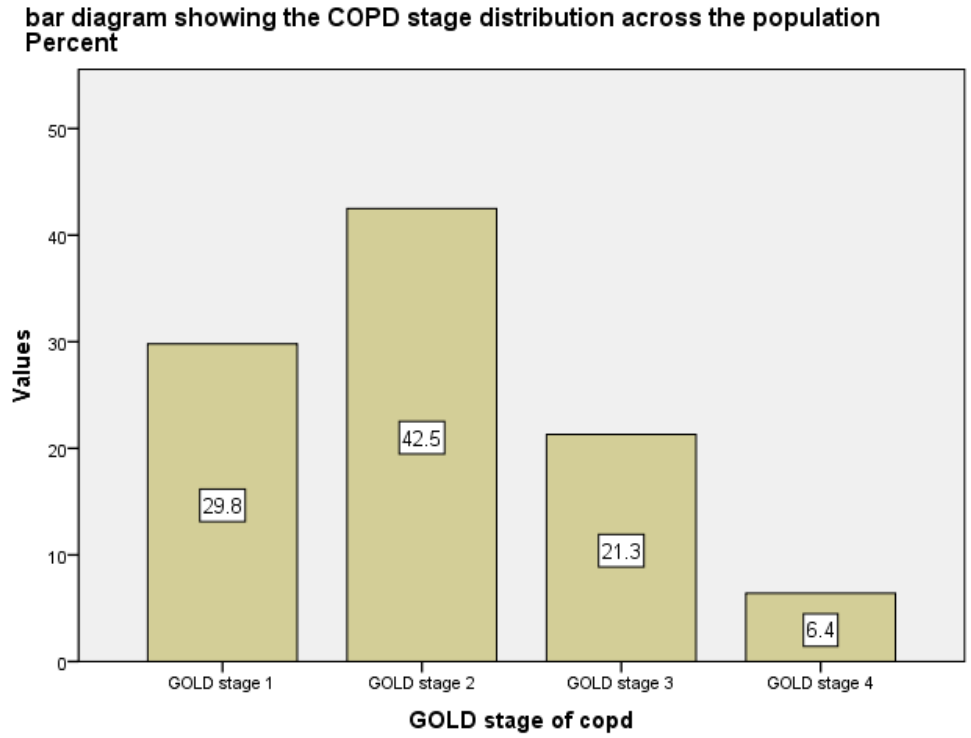

Figure 5 Stage of COPD distribution across study population

8.4.10 Chronic kidney disease (CKD)

- Chronic kidney disease (CKD) was defined as Crcl less than 60ml/min/1.73sq.m calculated with the abbreviated MDRD equation.
- About 73 patients (27.1%) were found to have evidence of CKD. 45 patients (61.6%) had stage 3 CKD , 21 patients (28.8%) had stage 4, and only 7 (9.6%) had stage 5 CKD.
- Of the 7 patients with stage 5 CKD, 2 were diabetes related, 1 was HTN related, 2 were connective tissue disease (CTD) related (both were microscopic polyangitis related) and 2 were due to NSAID abuse.
- Of the 7 patients, only 2 required maintenance dialysis, with one using haemodialysis and the other using peritoneal dialysis.
- Complications of CKD were widely seen in our study population with normocytic anaemia being very common, seen in 76.7% of the patients, followed by hyperuricemia in 52.1%, hyperkalaemia in 34.2% and hyperparathyroidism in 32.9%.This is summarised in Table 7.

Table 7 Statistics of chronic kidney disease in study population

Chronic kidney disease statistics	Frequency	Percent
a) Stage 3 CKD	45	61.6
b) Stage 4 CKD	21	28.8
c) Stage 5 CKD	7	9.6
stage 5 CKD on maintenance haemodialysis	1	14.2
Stage 5 CKD on maintenance peritoneal dialysis	1	14.2
Complications of CKD		
a) With normocytic anaemia	56	76.7
b) With secondary hyperparathyroidism	24	32.9
c) With hyperkalaemia	25	34.2
d) With hypernatremia	0	0
e) With hyponatremia	10	13.7
f) With hypercalcemia	3	4.1
g) With hyperphosphatemia	10	13.7
h) With hyperuricemia	38	52.1

i)	With metabolic acidosis	18	24.7

8.4.11 Chronic liver disease

- Eleven patients (3.9%) had evidence of chronic liver disease. Of these, 4 had evidence of portal hypertension with decompensation.
- The signs of decompensation and portal hypertension seen in these patients were as follows - all 4 had hypoalbuminemia, 3 had coagulopathy with no active bleeding, 2 had jaundice, 2 had splenomegaly and variceal bleed and hepatic encephalopathy were seen in 1 patient each.
- No patient underwent Trans jugular intrahepatic Porto systemic shunt (TIPS) or liver transplantation.

8.4.12 Thyroid disorders

- Forty patients (14.3%) had hypothyroidism. None of the patients had hyperthyroidism in our study group.
- Of these 40, 37 had primary hypothyroidism, and the other 3 resulted from varied causes - one patient initially had Graves' disease, post RAI, resulting in hypothyroid state. Another patient developed hypothyroidism post total thyroidectomy for multinodular goitre (MNG) thyroid. The last one resulted as a side effect to lithium, used for bipolar disorder.

8.4.13 Peripheral vascular disease

- Total of 6 patients (2.1%) had evidence of peripheral artery disease out of which 3 patients had arterial non healing ulcers, and 2 had undergone toe amputation.
- One of the persons, who underwent amputation of the toe, had also had a popliteo - tibial bypass.

- Interestingly all these 6 patients were non-smokers and all had DM, HTN, DL and three of them also had evidence of CAD.

8.4.14 Epilepsy

- Six patients (2.2%) had an epileptiform disorder, out of which only one was a primary epileptiform disorder and the others were all late onset seizures.
- Of these 5 patients with late onset seizure, 4 were of ischaemic etiology and 1 was secondary to a structural cause (cavernoma).

8.4.15 Intracranial (IC) bleed

- Only 9 patients (3.2%) had a history of intracranial (IC) bleeding, which included 6 hypertensive intracerebral bleeds, 2 subdural bleeds (SDH) and 1 subarachnoid bleed.
- Of the 2 persons with SDH, 1 had chronic SDH which was managed conservatively and the other patient had acute on chronic SDH, which was evacuated surgically. All 9 IC bleeds were non traumatic in nature.

8.4.16 Syncopal attack

- 5 patients had episodes of syncope with a mean of 2 episodes in a year. Of these 5 patients, 2 had neurogenic type of syncope, 1 had cardiogenic syncope and the other 2 were undiagnosed.
- None of them underwent pacing procedure.

8.4.17 Dementia

- Dementia diagnosed based on DSM 4, was seen in 40 patients (14.3%). Of these, 15 patients had Behavioural and psychological symptoms of dementia (BPSD).
- The commonest dementia type seen was vascular dementia, which accounted for 57.9%, followed by mixed and Parkinson's related dementia which accounted to

10.5% each respectively, pure Alzheimer's dementia in 7.9%, and other causes in 13.2%.

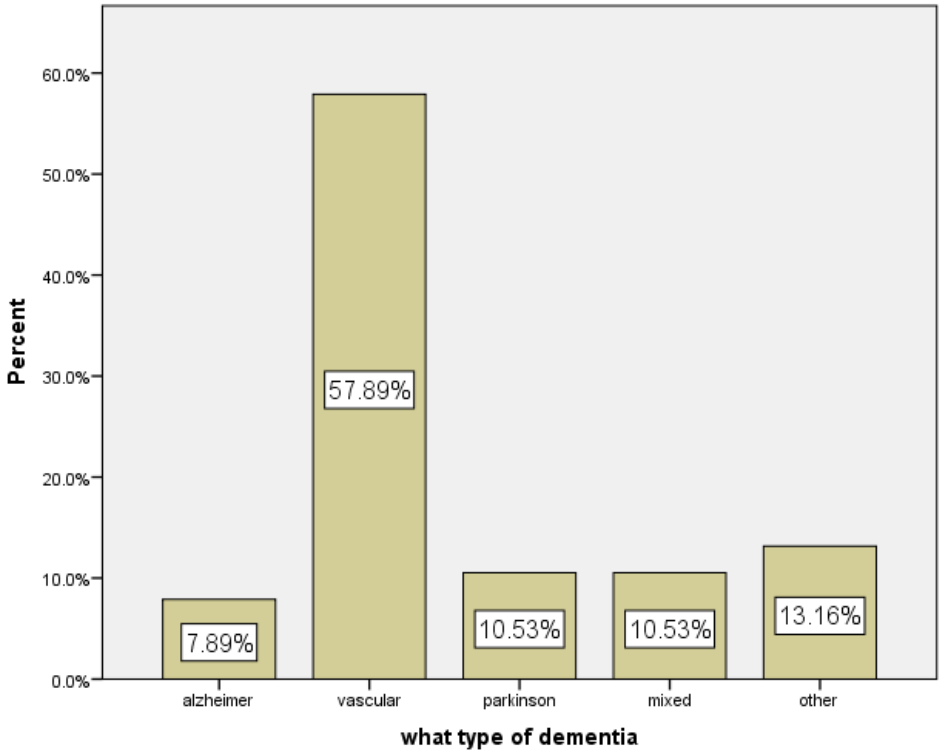

Figure 6 Type of dementia in study population

8.4.18 Parkinson's disease

- 32 patients had Parkinsonism, out of which 18 had primary Parkinson's and 14 had Parkinson's plus syndromes. 8 patients had idiopathic Parkinson's, 8 had vascular Parkinson's, 2 had antipsychotic related Parkinson's, and 14 had Parkinson plus types.
- Out of these 14 Parkinson plus variants, 6 had multisystem atrophy- Parkinson's type (MSA-P), 3 had multisystem atrophy cerebellar type (MSA-C), 4 had progressive supranuclear palsy (PSP) and 1 had Lewy body dementia. No cases of Shy Drager syndrome and corticobasal degeneration were identified.

8.4.19 Major Psychiatric disorder

- Totally about 9 patients (3.2%) had a major psychiatric disorder. This comprised 1 bipolar disorder, 1 depression with delusional thought and evolving psychosis, 2 adjustment disorder, 2 anxious personality trait, and 3 dysthymia.

8.4.20 Others CNS disorder

- We had 2 cases of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), and one case each of critical illness polyneuropathy , Mitochondrial encephalopathy, lactic acidosis and stroke like syndromes(MELAS) , myasthenia gravis, Normal pressure hydrocephalus (NPH), Dural arteriovenous(AV) fistula involving cord causing paraparesis and motor neuron disease.

8.4.21 Haematological disorder

- 16 patients had primary haematological disorders. None of them had bone marrow transplantation. This is summarised in table 9.

Table 8 Distribution of various haematological disorders in study population

Haematological disorder	Frequency	percentage
Hodgkin lymphoma	1	0.4
Non-Hodgkin's lymphoma	1	0.4
Leukaemia	1	0.4
Plasma cell dyscrasia	7	2.5
Beta thalassemia trait	1	0.4
MDS	3	1.1
Myelofibrosis	1	0.4
Polycythaemia Vera	1	0.4

8.4.22 Malignancy

- About 29 patients (10.4%) had some form of malignancy and 13 had evidence of systemic metastases. The various types of malignancy and the distribution among our study population are summarised in table 10.
- Of these 29 patients, only 21 patients received treatment. In treated people, 6 were treated with chemotherapy, 8 received some form of surgical intervention and 7 received both chemotherapy and surgery with or without radiotherapy.

Table 9 Distribution of various types of malignancy among our study population

Primary malignancy	Frequency	Percentage
Gastrointestinal tract(GIT)	7	2.5
Lung	2	0.7
Genitourinary	5	1.8
Skin and soft tissue	1	0.4
Haematological	8	2.9
Breast	2	0.7
Cervix	1	0.4
Hard palate	1	0.4
Thyroid	1	0.4
Parathyroid	1	0.4

8.4.23 Connective tissue disorder (CTD)

- Totally about 21 patients (7.5%) had CTD. Of these, 18 cases had significant major organ involvement and all these 18 patients were receiving some form of immunomodulation therapy.

Table 10 Connective tissue disorder distributed among our population

Connective tissue disorder	Frequency	Percentage
Rheumatoid arthritis	5	1.7
SLE	2	0.7
MCTD	2	0.7
Systemic sclerosis	1	0.4
Sjogren's syndrome	1	0.4
Sarcoidosis	1	0.4
p- ANCA positive vasculitis	4	1.4
Rapidly progressive glomerulonephritis (RPGN)	2	0.7
Still's disease	1	0.4
Sernegative sponyloarthritis	1	0.4

8.4.24 Dermatological disorder

- About 19 patients (6.8%) had some form of dermatological disorder. The various diseases identified are mentioned in table 11.

Table 11 Distribution of various dermatological disorders in the study population

Dermatological disorder	Frequency	Percentage
Atopic dermatitis	2	0.7
Contact dermatitis	1	0.4
Dermatitis herpetiformis	1	0.4
Discoid eczema	1	0.4
Lower limb eczema	2	0.7
Lichen planus	4	0.4
Pemphigus vulgaris	1	0.4
Psoriasis	3	1.1
Vitiligo	2	0.7
Asteatotic eczema	2	0.7

8.4.25 Other diseases

- There were 2 patients with hepatitis B and 2 with hepatitis C infection. One among the 2 hepatitis C infected patients was on treatment with antiviral drugs.
- In males, 33% had prostate enlargement, out of which half the number was of a higher grade of prostatism. Only 11 out of 45 patients with severe prostatism has underwent transurethral resection of prostate (TURP).
- In females, urethral stenosis was present in 2 people; of which one underwent dilatation. Unfortunately both the females were having recurrent urinary tract infections (UTI), and were not on long term antibiotic prophylaxis.

8.4.26 Incontinence

- Another significant concern was incontinence, which was present in 20.4% (57) of the population, with functional incontinence in 35%, urge incontinence in 29.6%, mixed type in 15.8%, followed by stress incontinence in (10.5%) and overflow incontinence in 8.5%.
- Recurrent UTI was seen in a significant population, with a total of 28 cases. Out of 28 people, only 8 (28.5%) were on long term antibiotic prophylaxis.
- Interestingly one of the risk factors apart from female sex, and obstructive uropathy, found was indwelling catheter. A total of 12 patients were found to have indwelling catheter.

8.4.27 Osteoarthritis

- More than 60% of population were suffering from some form of degenerative joint disease. 28 patients were found to be chronic users of non-steroidal anti-inflammatory drugs (NSAIDs), with pain being the main reason attributed by these patients for the abuse of NSAIDs. The most commonly affected joints being the knee 55.6%, lumbar

spondylosis 41%, cervical spondylosis 18%, hip 2.5% and Diffuse Idiopathic Skeletal Hyperostosis (DISH) 1.4%.

- About 68 percent were diagnosed previously to have osteoporosis by DEXA scan, and 32 people had suffered a fragility fracture in the past. But out of these 100 people, only 19 patients were already on bisphosphonates.

8.4.28 Charlson comorbidity index

- A mean score of 6 ± 2, with a range of 2 to 14 was identified in our study population, meaning that the population that we are studying was highly complex with multiple comorbidities. There was no gender and age subclass variation. (figure 7)

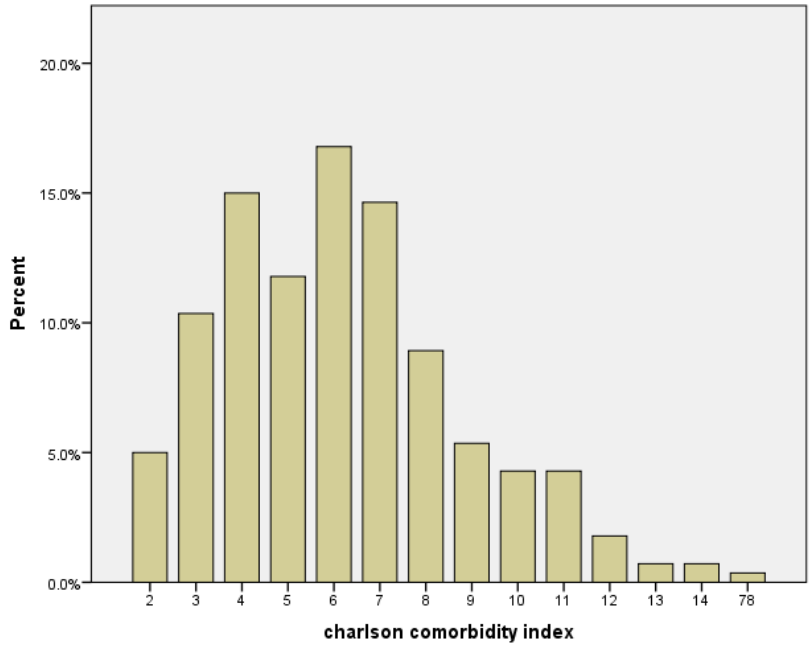

Figure 7 Distribution of Charlson comorbidity index

8.5 Factors affecting drug intake and absorption

a) **<u>Swallowing impairment :</u>** About 8% of the population had swallowing impairment, out of which 1 patient had a structural defect in the form of carcinoma(CA) larynx, 5

had severe reflux symptoms and the rest were due to neurological impairment and poor cognitive status.

b) **Gastro-oesophageal reflux disease(GORD)** A significant number (about 20 people) had severe GORD with evidence of hiatus hernia in recently done upper gastrointestinal(GI) scopies

c) **CONSTIPATION** A major chunk of the population (about 71%) was suffering from symptomatic constipation, which warranted them the use of laxatives at some point in their life.

d) **DIARRHOEA** 4 patients in our study had increased frequency of stools secondary to irritable bowel syndrome, and these patients were on more than one antidepressant.

e) **HISTORY OF GI SURGERY** A total of 5 patients had a history of extensive bowel resection surgeries in the past. It included 2 distal gastrectomies for stomach cancer, 2 gastrojeunostomies and 1 small bowel resection.

1) CREATININE

The mean value of creatinine was found to be 1.2 ± 1.03, and it ranged from 0.3 to 8.3. The mean creatinine clearance (Crcl) found using Cockcroft Gault equation is 53.8 ± 22 and Crcl using abbreviated MDRD was 73.5 +/- 33.About 75 patients (26.8%) were found to have crcl < 60ml/min/m^2. The distribution of creatinine clearance is shown below as a histogram, and the creatinine class distribution is tabulated in table 12.

Table 12 Stages of CKD in study population (KDOQI guidelines)

Stage of CKD	Frequency	Percentage
Stage 1	82	29.3
Stage 2	111	39.6
Stage 3	49	17.5

Stage 4	18	6.4
Stage 5	8	2.9

2) SERUM ALBUMIN

The mean albumin level was found to be 3.5 ± 0.6, ranges from 1.6 to 4.9.

3) Body mass index(BMI)

The mean height was 162cm ± 7 cm, ranging from 135 to 182 cms. The mean weight of the population was 65kg ± 13kg. The mean BMI was calculated to be 24.9 ±5, which ranged from 13 to 44 kg/sq. m. Normal BMI was seen in 48.9%, underweight in 6.8%, overweight in 30% and obesity in 14.2%. (table 15)

Table 13 BMI distribution in study population

Stage	BMI	Frequency	Percentage
Under weight	Less than 18.4	19	6.8
Normal	18.5 to 24.9	137	48.9
Over weight	25 to 29.9	84	30
Obese class 1	30 to 34.9	27	9.6
Obese class 2	35 to 39.9	9	3.2
Obese class 3	More than 40	4	1.4

8.6 OUTCOMES

8.6.1 Prevalence of PIM use

- In our study of 280 patients, 276 patients (98.6%) were using regular drugs.
- In these 276 participants, a total of 1790 drugs were prescribed, out of which 350 drugs (19.5%) were considered inappropriate according to Beers´ criteria.
- Of the 350 inappropriate drugs, 118 were considered to be class I PIM, 188 class 2 PIM and 44 were class 3 PIM drugs.
- The use of at least one PIM drug was seen in 93 (33.2%) patients.

- Most patients were found using one PIM drug (71%), 21.5% were using 2 PIM and a small proportion was using more than 2 PIM (7.5%)
- Table 16 list all the inappropriate drugs identified with Beers´criteria.

Table 14 Prevalence of PIM according to Beers´ criteria

PIM – Beers´ criteria	Numbers	% of 280 pt
Prevalence of PIM users	93	33.2
• 1 PIM user	66	23.6
• 2 PIM user	20	7.1
• > 2 PIM user	7	2.5
	Number of drugs out of 350 with percentage	
PIM class 1 drugs	118	33.7
1. Central nervous system drugs:		
a) Benzodiazepines (percentage among class 1 PIM drugs)	23	6.6
	16	4.6
b) Conventional antimuscarinics	14	4
c) Antipsychotics	10	2.9
d) Tricyclic antidepressants	2	0.6
e) Non BZD hypnotic	1	0.3
f) Barbiturates		
2. Cardiovascular system drugs:		
a) Antiplatelets other than aspirin / clopidogrel	1	0.3
b) Alpha blockers	4	1.1
c) Central alpha agonist	5	1.4
d) Spironolactones > 25 mg per day	7	2
e) Digoxin more than 0.125mg per day	4	1.1
f) Anti arrhythmics	4	1.1
3. Others		
a) Long acting sulphonyl urea	4	1.1
b) Estrogen	1	0.3
c) 1st generation antihistaminics	7	2
d) Mineral oil	2	0.6
Prevalence of class 2 PIM (to be avoided in specific disease condition)	188	53.7

1. In heart failure		
a) NSAID	6	1.7
b) Amiodarone	3	0.9
c) Verapamil	1	0.3
d) Cilostazol	1	0.3
2. In syncope		
a) Acetyl cholinesterase inhibitors	1	0.3
b) Alpha blockers	1	0.3
3. History of fall / fractures		
a) Anticonvulsants	20	5.7
b) Benzodiazepines	16	4.6
c) Antipsychotics	14	4
d) TCA	4	1.1
e) SSRI	3	0.9
4. In epilepsy		
a) olanzapine	2	0.6
5. History of delirium		
a) Anticholinergics	10	2.9
b) Benzodiazepines	7	2
c) Non BZD hypnotic	2	0.6
d) TCA	2	0.6
e) H2 antihistaminics	4	1.1
6. In dementia		
a) Anticholinergics	8	2.3
b) Antipsychotics	11	3.1
c) Benzodiazepines	4	1.1
d) H2 antihistaminics	1	0.3
7. In parkinsonian disorder		
a) Antipsychotics other than quetipatine or clozapine	3	0.9
8. In insomnia		
a) Theophyllines	3	0.9
9. In constipation		
a) Anticholinergics	12	3.4
b) Antipsychotics	14	4
c) TCA	11	3.1
d) 1st generation antihistaminics	4	1.1
e) Non dihydropyridine	3	0.9
10. In gastric ulcer		
a) NSAIDs other than low dose aspirin	4	1.1
11. History of urinary incontinence		
a) Alpha blockers	2	0.6

12. In symptomatic BPH		
a) Anticholinergics	11	3.1
Prevalence of class 3 PIM (to be used with caution in elderly)	44	12.6
1. Primary prophylaxis with antiplatelet for patient > 80 yrs (percentage among class 3 PIM users)	5	1.4
2. Usage of SIADH prone drugs		
a) Antipsychotics	14	4
b) TCA	10	2.9
c) SNRI	8	2.3
d) SSRI	4	1.1
e) Carbamazepine	4	1.1
f) Glibenclamide	4	1.1
Total	350	100

8.6.2 CLASS 1 PIM - *(Drugs to be avoided in elderly , irrespective of underlying disease)*

a) Drugs with anticholinergic activity

- A total of 60 patients (21.4%) had been exposed to anticholinergic drugs and about 73 drugs with anticholinergic activity (20.9%) were spotted with Beers´ criteria and Jag, 2008.
- Beers´ criteria picked up 47 drugs (13.4%) with anticholinergic activity, and Chew et al, review article helps to spot an additional 26 drugs (7.4%) with anticholinergic activity, which were declared unsafe to use in elderly.
- Out of 14 drugs with anticholinergic activity identified with the Beers´ criteria 34% were antimuscarinics, 30% antipsychotics, 21.3% TCAs, and 15% were 1st generation antihistaminics.
- Out of 16 conventional antimuscarinics drugs, half the number was trihexyphenidyl, a centrally acting anticholinergic antiparkinsonian drug.

- Out of 14 antipsychotics identified, only 2 were typical antipsychotics and the rest were newer atypical antipsychotics. In the atypical group, quetiapine is the major contributor. Out of 10 TCAs identified, 9 were amitriptyline.
- More than 2/3rd of drug with anticholinergic activity was contributed by 4 drugs - Trihexphenidyl, Amitriptyline, Quetiapine and Risperidone.
- Another 26 drugs were additionally identified with Chew et al (31) and these are listed in table 18.
- The commonest ADEs requiring hospitalisation observed with anticholinergic drugs are SIADH in 6 patients, followed by SAIO in 2 patients and delirium and fall in one patient each.

Table 15 Drugs with anticholinergic activity to be avoided, according to Beers´ criteria, 2012

Muscarinic receptor antagonist	**counts**	**percentage**
1. Central acting anticholinergic – antiparkinsonian drug		
a) Trihexyphenidyl	8	2.3
2. Antispasmodic agent		
a) Dicylomine	1	0.3
b) others	1	0.3
3. Other anticholinergics	6	1.7
Antipsychotic		
1. Typical		
a) Haloperidol	1	2.1
b) Trifluperazine	1	2.1
2. Atypical		
a) Quetiapine	8	2.3
b) Risperidone	4	1.1
Tricyclic antidepressant		
- Amitriptyline	9	2.6
- Other TCAs	1	0.3
1st generation Anti histaminic	7	2
Total	47	13.4

Table 16 Drugs with anticholinergic activity to be avoided, according to Chew et al(31)

Drug	Counts	`Percentage
Tolterodine	2	0.6
Olanzapine	3	0.9
Escitalopram	4	1.1
Fluoxetine	1	0.3
Mirtazapine	7	2
Ranitidine	9	2.6
Total	26	7.4

b) Sedatives

- Totally 26 sedatives were identified.
- Out of these, benzodiazepines were found to be the predominant tranquilizers used (88.5%), which included 5 on alprazolam , 6 on lorazepam , 11 on clonazepam and only one on diazepam.(table 19)
- Amongst the 5 alprazolam users, one had a fall.
- We had 1 patient who died in hospital due to respiratory depression 2* to midazolam that was used as an IV sedative while doing a procedures.

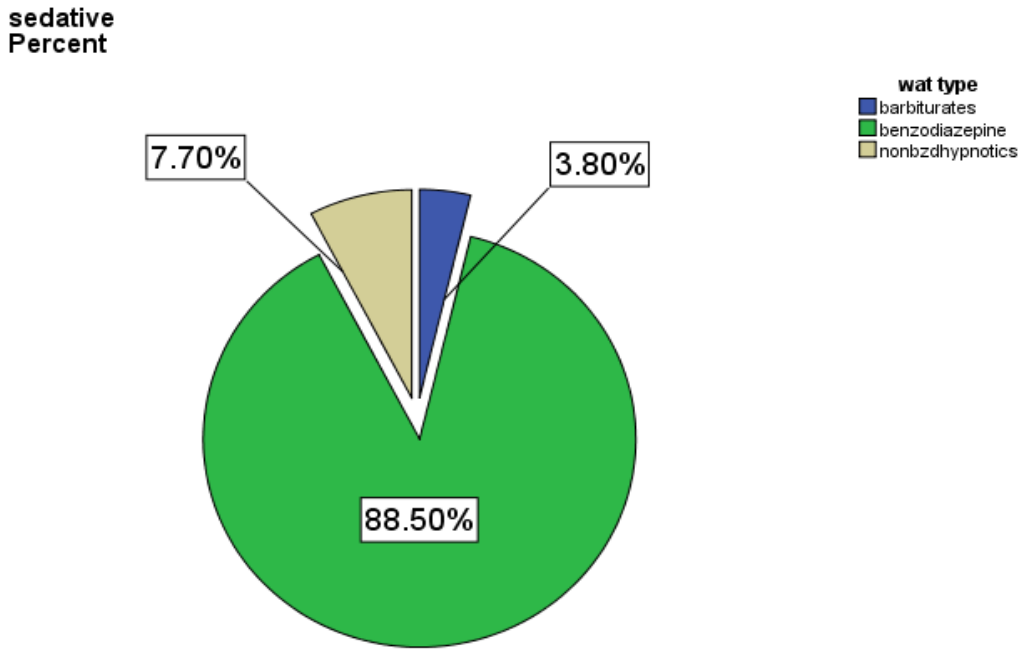

Figure 8 Type of Sedative used by our study population

Table 17 List of sedatives used by our study population

1. **Benzodiazepine**	**Numbers**	**Percentage**
a) Short acting BZD		
i. Alprazolam	5	1.4
ii. Lorazepam	6	1.7
b) Long acting BZD		
i. Clonazepam	11	2
ii. Diazepam	1	0.3
2. Non BZD hypnotic - Zolpidem	2	0.6
3. Barbiturates	1	0.3
Total	26	7.4

c) Antiplatelets other than aspirin and clopidogrel

- Only one patient was found using prasugrel as his antiplatelet agent post CAD. He was using prasugrel 10mg once daily as secondary prophylaxis for CAD and there was no ADE or bleeding diathesis reported.
- No ticlopidine and dipyramidole use was detected.

d) Alpha blockers

- Four patients were using prazosin, an alpha blockers as their hypertensive. Amongst these 4 users, 3 had reasonable indications justifying its use,
- 1 patient had refractory hypertension with multiple drugs and
- 2 patients had CKD with crcl <30.
- But in 1 patient, prazosin was inappropriately used as the initial choice of antihypertensive which resulted in symptomatic postural hypotension and hospitalisation.

e) Central alpha agonist

- Five patients were found using a central alpha agonist - among them 4 were using clonidine and 1 was using moxonidine.
- The person who was on moxonidine was found to be using 5 different antihypertensive agents for essential benign hypertension and got admitted with pedal oedema, which was contributed to by the higher dose of moxonidine and resolved after withdrawing moxonidine.

f) Spironolactone > 25mg/day

- High dose spironolactone was used by 7 patients.
- Out of these 7 patients, no patient has an absolute indication for its use.
- It was used inappropriately in 3 patients having chronic liver disease with reduced creatinine clearance.

- In 2 patients with CAD, spironolactone was inappropriately used as there was no evidence of cardiac dysfunction.
- We identified 2 patient admitted with hyperkalaemia 2* to high dose spironolactone us - one was using 50mg daily along with ACEI for CAD with no failure, and other was using the same dose in CLD with reduced creatinine clearance.
- We also reported one case with acute kidney injury with spironolactone usage.

g) Antiarrhythmic drugs

- Anti-arrhythmic drugs were used by 4 patients and all of them were on amiodarone.
- Three patients were using it for atrial fibrillation, and 1 was using amiodarone following cardiac arrest after ventricular fibrillation.
- Out of these 4 users, 1 developed drug induced hypothyroidism and the other went into cardiac arrest which required TPI placement.

h) Digoxin more than 0.125mg per day

- Digoxin at higher dose (>0.25mg per day) was given to 4 patients.
- Only 2 had atrial fibrillation with failure, which is an absolute indications for its use. The other 2 did not have absolute indication for the use and in fact , one among them used digoxin at a higher dose with a crcl of only 40ml/min with no evidence of failure clinically or ECHO report wise.
- No electrolyte abnormailties were identified

i) **Long acting sulphonyl urea**

- Only 4 patients out of 156 diabetics were found using glibenclamide and no chlorpropamide users detected.
- All these patients had normal renal functions and no hypoglycaemic episodes or SIADH were reported in these patients.

j) One patient was found to be using oral oestrogen for post-menopausal symptoms. No thromboembolic episodes were seen with oestrogen use

k) Two patients were found using mineral oil as a laxative.

Table 18 PIM drugs mentioned in Beer´s criteria

	PIM drugs mentioned in Beers´ criteria	Number	percentage
i.	Antiplatelets other than aspirin and clopidogrel	1	0.3
ii.	Alpha blockers – prazosin	4	1.1
iii.	Central alpha blockers		
	- Clonidine	4	1.1
	- Moxonidine	1	0.3
iv.	Antiarrhythmics – amiodarone	4	1.1
v.	Spironolactone > 25mg / day	7	2
vi.	Digoxin > 0.125mg/day	4	1.1
vii.	Glibenclamide	4	1.1
viii.	Oestrogen	1	0.3
ix.	Mineral oil	2	0.6
x.	Others		
	- Nifedipine immediate release	0	0
	- Sliding scale insulin use		
	- Pethidine		
	- Pentazocine		
	- skeletal muscle relaxant and ergot derivative		
	- Androgen and megestrol		
	- Dessicated thyroid preparation		
	- Growth hormone		
	- Metaclopromide		

The most common inappropriate class 1 drug found in our study was drugs having anticholinergic activity (13.4%) followed by sedative group of drugs (7.4%) of PIM and cardiovascular drugs (7.1%), which mainly included inappropriately dosed spironolactone & digoxin.

8.6.3 CLASS 2 PIM *(Drugs not to be used in specific disease conditions)*

a) History of heart failure

- In 91 patient with heart failure, 6 was found using NSAID, 1 using verapamil, and 1 cilostazol user was found. No patient was prescribed any thiazolidinedione or dronedarone. But 3 patients with heart failure were prescribed with amiodarone.

b) History of syncope

- We had 9 patient with syncopal episodes, and one was found using prazosin, one was using acetylcholinestrase inhibitor
- No users TCAs, typical antipsychotics identified.

c) History of falls with or without fractures

- A larger fraction of the study population, about 148 out of 280, has a history of falls with or without fractures.
- Out of these people, 20 were found to be using anticonvulsant, 16 using BZD, 14 using antipsychotics, 4 using TCA & 3 using SSRI.

d) History of epilepsy

- In 7 patients with epilepsy, 2 was found using olanzapine.
- No chlorpromazine, thioridazine, thiothexene, clozapine, bupropion or tramadol users were found.

e) History of delirium

- Totally 105 patients had experienced delirium in the past.
- Out of this cohort, 10 were found to be using anticholinergics, 7 using BZD, 2 using zolpidem, 2 using TCA users and 4 using ranitidine.
- No chlorpromazine, thioridazine, Pethidine or steroid use was found.

f) History of dementia

- 44 patients had major neurodegenerative disease.
- Amongst them 8 were found using anticholinergics, 11 using antipsychotics, 4 using sedatives and 1 was using ranitidine.

g) History of parkinsons disorder

- 32 people were found to have some form of parkinsonian disorder, amongst them 3 were using antipsychotics other than quetipatine or clozapine.
- No anti emetics like metoclopramide, prochlorperazine, promethazine were used by these patients.

h) History of insomnia

- 74 people in our study group has disturbed sleep, and among these , 3 were using theophyllines, but no oral decongestants, stimulants, caffeine use was found.

i) History of constipation

- More than 70% (199) of the population had constipation, out of which 12 were using antimuscarinic agents , 14 antipsychotics, 11 TCAs, 3 non dihydropyridines and 4 first generation antihistaminics were found.

j) History of gastric ulcer

- A total of 20 patients has endoscopy proven gastric ulcer and amongst them, 4 were found using NSAIDs other than low dose aspirin.

k) History of urinary incontinence

- Urinary incontinence was seen in 65 people and 2 patients were found using prazosin.

l) History of lower urinary tract symptoms in BPH

- Ninety three males were found to be having symptomatic BPH, out of which 11 patients were oral anticholinergic drugs users, were found.
- Surprisingly, no males with BPH with LUTS were found using any form of Metered Dose Inhaler (MDI) with anticholinergic activity

Out of total 350 inappropriate drugs, 188 drugs were identified to be inappropriate when used in specific disease conditions. The commonest drug – disease interaction found in our study was using major and minor tranquilizers in the setting of fall, delirium and dementia, which constitutes 28.7%, followed by drugs with anticholinergic activity in patients with delirium, dementia, constipation and symptomatic LUTS, which constitutes 21.9% of drug – disease interactions.

8.6.4 CLASS 3 PIM *(Drugs to be used with caution in elderly)*

a) **Age more than 80 years**

- Totally about 30 patients were above the age of 80years.
- 5 patients were found using aspirin for primary prevention of cardiac events.
- No patient in this age group was prescribed prasugrel for same indications

b) Usage of SIADH prone drugs in elderly

- The entire population was above 60 years of age, out of which 14 antipsychotics, 10 TCAs, 8 SNRIs, 4 SSRIs, 4 carbamazepine and 4 glibenclamide users were found.

- No patient was found using chlorpropamide ,vincristine, carboplatin or cisplatin.
- A total of 8 patients required hospitalisations for symptomatic SIADH with hyponatremia due to these drugs.

c) <u>In elderly more than 60 years with history of syncope</u>

- In our study group, 9 patients had history of syncope and no one was exposed to any of the direct arteriolar or venous dilatators.

The number of drugs to be used with caution was identified as 44.

<u>Prevalence of renally inappropiate drugs according to Beers´ criteria</u>

a) <u>Nephrotoxic drug</u>

- Totally 12 patients were currently using NSAIDs.
- And 28 people had a history of NSAID use for more than 2 weeks, in the past.
- Out of these 12 patients, diclofenac was used by 3 people, ibuprofen by 1, and rest were on other NSAIDs.
- No triamaterene use was found in our study population.

b) <u>Drugs which require dose adjustment according to crcl</u>

- In patients with crcl < 60ml/min, 3 patients were using nitrofurantoin
- In patient with crcl < 30 ml/min, only one patient was found using spironolactone and no patient was found using prasugrel in stage 5 CKD.

c) <u>Number of renally inapprropiate drugs</u>

- Totally 16 Renally inappropriate drugs (5.7%) were identified with the help of Beers´ criteria, however more number of RIM identified on application of hanlol et al criteria.

Table 19 prevalence of renally inappropriate drugs in our study population

	Numbers	Percentage
Prevalence of renally inappropriate drugs , according to Beers´ criteria only	16	5.7
Prevalence of renally inappropriate drugs , according to Beers´ criteria plus hanlon et al	60	21.4

Renally inappropiate drugs according to Hanlon et al

Nephrotoxic drugs

A total of 11 nephrotoxic drugs are identified.

Table 20 Renally inappropiate drugs according to Hanlon et al(32)

Nephrotoxic drugs	Count	percentage
Aminoglycoside	3	27
Amphotericin	2	18
Cisplatin	1	9
Cyclosporin	1	9
Lithium	2	18
Gold salts or pencillamine	1	9
IV radiographic contrast	1	9

Drugs to avoid if crcl <30

Table 21 drugs to avoid if crcl < 30 according to hanlol et al(32)

Drug /drug class to avoid,if crcl < 30	Count	Percentage
Long acting sulphonyl ureas	5	1.8
Hydrochlorthiazide	3	1.1
Bisphosphonates	0	0
Cotrimoxazole	0	0
Ciprofloxacin > 500mg/day	0	0
Acyclovir > 800 Q8H	0	0
Allopurinol > 200mg /day	0	0
Cetrizine > 5mg /day	0	0

Memantine > 5mg BD	0	0
Metoclopromide	0	0
Colchicine	0	0
Pethidine	0	0
Propoxyphene	0	0

Drugs to be avoid if crcl < 60ml/min

Table 22 Drugs to be avoid if crcl < 60ml/min, according to hanlol et al**(32)**

Drug /drug class to avoid,if crcl < 60	**Count**	**Percentage**
Metformin	19	6.8
Amantadine > 100mg / day	1	0.4
Gabapentin for pain > 600 BD	0	0
Ranitidine >150mg / day	5	1.8
Valcylovir >1g Q12H	0	0

8.6.6 Prevalence of polypharmacy and excessive polypharmacy

The mean number of drug used by our study population was 6 ±4 drugs, the number ranges from 1 to 21 drugs. The histogram shown below depicts the distribution of number of drug intake in our study population. Out of 280, 153 patients (53.9%) were using more than 5 drugs per day, and 44 patients (15.7%) were using more than 10 drugs per day.

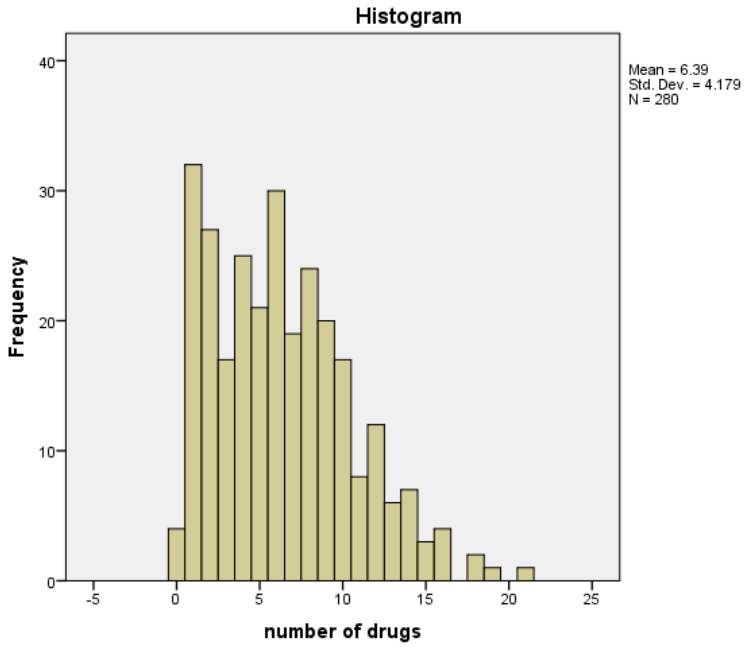

Figure 9 Histogram showing the distribution of number of drugs used per individual

Table 23 Table showing the prevalence of polypharmacy and excessive polypharmacy

	Numbers	Percentage
Mean number of drug 6 ± 4 , range 1 to 21 drugs		
Prevalence of polypharmacy	153	53.9
Prevalence of excessive polypharmacy	44	15.7

List of complementary and alternative medicines

List of CAM	Counts	Percentage
Calcium	43	15.6
Vitamin B12	16	165.7
Multivitamin	16	5.7
Antioxidants	2	0.7
Neuroprotectors	2	0.7
Iron supplement	18	6.4
Cranberry	1	0.7
Papaverine for giddiness	1	0.7
Prevagen(brain supplement)	1	0.7
Ursodeoxycholic acid	3	1.1
N acetyl cysteine	2	0.7

Ayurvedic medicines	4	1.4
Heavy metals	4	1.4
Steroids in naïve treatment , with no absolute indication	9	3.2

- Significant proportions of patients were found using CAM and the list of CAM is listed in the table.
- In our study a total of a total of 355 essential drugs according to start criteria was not prescribed to the study population.
- And suprisingly only 30% of population was prescribed all essential drugs appropriately and remaining 70% of population has atleast one essential drug omitted.
- The most commonly omitted drug was identified as aspirin , followed by ACEI and beta-blockers post CAD.
- Drug / therapeutic duplication was seen in 12 patients and the various combinations were listed below:

TABLE 24 DRUG OMISSION SCREENED WITH START CRITERIA

Drug screening	Yes	No	% of omissions
Cardiovascular system			
1. Warfarin in chronic AF, with chad score >2	4	7	63.7
2. Aspirin in chronic AF, with chad score < 2	0	3	100
3. Aspirin post CAD	43	10	18.9
4. Aspirin in peripheral arterial disease	6	0	0
5. Statins in peripheral arterial disease	5	1	16.7
6. ACEI post CAD, with crcl >60	17	19	52.8
7. ACEI post CAD with heart failure, with crcl >60	15	8	34.8

8. Betablockers post CAD	35	18	34
9. Anti hypertensives, in hypertension (JNC8)	194	28	12.6
10. Statin in dyslipidemia (ATP3guidelines)	163	14	7.9
Endocrine system			
1. Metformin in DM, with crcl > 60	115	15	11.5
2. ACEI in DM nephropathy, with crcl > 60	9	15	62.5
3. Aspirin in DM	76	80	51.3
Respiratory system			
1. Inhaled β2 agonist /anticholinergic in moderate to severe COPD	36	28	43.8
2. Home oxygen in chronic type 1 respiratory failure	0	3	100
3. Not on CPAP in OSAS	3	9	75
Central nervous system			
1. L dopa in idiopathic parkinons	5	3	37.5
2. Depression with GDS 5/5, with insomnia > 3months	19	17	47.2
Gastrointestinal system			
1. PPI in chronic severe reflux	17	3	15
2. Laxative in chronic symptomatic constipation	92	20	19.6
Locomotor system			
1. DMARDs in Rheumatoid arthritis	4	1	20
2. Bisphosphonates in chronic steroid use > 1month	10	13	56.5
3. Bisphosphonates in osteoporosis, with crcl > 60	19	49	72.1

Table 25 Additional drug omissions, not defined by START criteria

Additional drug screening	Yes	No	% of ommission
1. Longterm antibiotic prophylaxis in recurrent UTI	8	20	71.4
2. Hypouricemic drugs for CKD related hyperuricemia	13	29	69.0
3. Phosphate binders for CKD related hyperphosphatemia	3	7	70

4. Drugs in CKD related secondary hyperparathyroidism	9	15	62.5
5. Drugs in symptomatic moderate to severe BPH	30	15	33.3
6. Vaccination in COPD	5	68	93.1
7. Cholinesterase inhibitors for alzeheimers dementia	3	2	40
8. Helicobacter pylori eradication therapy , when indicated	2	1	33.3
9. Treatment for multiple myeloma	3	4	57.1

Drug duplications:

list of duplicated drugs	Counts	Frequency
1. Gliclazide & glimepride	1	0.4
2. Frusemide & torsemide	1	0.4
3. Enalapril & valsartan	1	0.4
4. Metoprolol & atenolol	1	0.4
5. Rate controlling with verapamil, betablocker and digoxin in AF	2	0.7
6. Ranolazine, nitrates, nicorandil	2	0.7
7. valproate, phenytoin, clobazam	1	0.4
8. valproate,levetiracetam	1	0.4
9. Nicorandil, pentoxiphylline, cilostazol	1	0.4
10. Alprazolam, lorazepam	1	0.4

Other significant inappropriate prescribing found in our study

1. Using diuretics for treating pedal edema with no failure was seen in 3 patients
2. On both cholinergic and anticholinergic drugs was seen in 3 patients
3. Metformin in severe LV systolic dysfunction was seen in 1 patient

8.7 TREATMENT FACTORS

Of the 280 patients, a median of 2 doctors were treating each patient, with a maximum of 5 doctors in a few patients. The majority of the population (82%) was been treated by one or two doctors. Out of 280 patients, 99 patients (35.4%) has been seen by a geriatrician in addition to any other professional and 33 patients (11.8%) have been purely following a geriatrician. The majority of the population 67% was been treated by a general practioner. Of a total of 169 patients (60.5%) who were been treated by more than 1 doctor in about 132 (78%) , there was proper communication between their doctors, but in the remaining 37 patients the treating doctor did not have a proper accessibility to patients records. About 125 patients (44.6%) has been following up with their doctors frequently with atleast one visit every 3 months, and 67 patients (23.9%) were following up with their doctors atleast once every 6 months. About 45 (16%) of patients did not do regular check up previously, but had been following up with their doctors very frequently following their recent acute illness. A significant number of patients, about 15% were not under regular follow up. About half the population, about 46% needed to spend less than 500 rupees a month for their medicines, 30% needed to spend less than 1000 a month, and 20% of the population needs a larger sum (> 1000 a month) for their medicines. About 30 patients in our study group reported to have self-medication use, and the majority of the time it was NSAIDS, cough syrup, paracetamol and laxatives, dominating the list. Majority of the population (85%) was found to be compliant to the drugs. Only 17 patients in our study group had a good understanding of their disease status and the drugs they were taking, and only 26 patients know how to use a drug dosette. More than 30% of population could not take their medicines themselves and requires another person help.

8.8 Details of past ADR

A total of 31 patients had reported 33 different ADEs in the past. Out of which no patient died. 4 patients required ICU hospitalisation. Out of these 33 events, 7 were managed on an OPD basis and the other 26 required hospitalisation, with 3 requiring ICU care, but no one succumbed to the illness. Out of the 33 ADEs, 9 were drug related dyselectrolytemias. Hyponatremia is the most common dyselectrolytemias.

Table 26 Details of past adverse drug events

	Details of past ADR	Counts	Percentage
1.	Drug related dyselectrolytemia		
	a) Dehydrational hyponatremia		
	i. Loop diuretic	2	0.6
	ii. Thiazide	1	0.3
	b) SIADH with hyponatremia		
	i. Antidepressants (amitriptyline, fluoxetine, mirtazapine)	3	0.9
	ii. Carbamazepine	1	0.3
	c) Hypokalemia – loop diuretic related	1	0.3
	d) Hyperkalemia – ACEI related	1	0.3
2.	Hypoglycemia		
	a) Actrapid	1	0.3
	b) Mixtard (30 /70)	1	0.3
	c) Sulphonyl urea – Gliclazide	1	0.3
3.	Transaminitis		
	a) Emprical ATT related	1	0.3
	b) Valproate related	1	0.3
4.	Rifampicin (empirical ATT) cholestatic jaundice	1	0.3
5.	Pancreatitis – tamoxifen related	1	0.3
6.	Nifedipine related pedal edema	1	0.3
7.	Verapamil related SAIO	1	0.3
8.	Amantadine related postural hypotension	1	0.3
9.	Delirium		
	a) Ropinirole	1	0.3
	b) Gabapentin	1	0.3
10.	Inappropiate anticoagulation - Haematuria due to overanticoagulation	1	0.3
11.	Lithium related hypothyroid	1	0.3
12.	Amiodarone related complete heart block and arrest requiring TPI	1	0.3
13.	Tamoxifen related endometrium carcinoma	1	0.3

14. Osteoporosis		
a) Valproate	1	0.3
b) Lithium	1	0.3
15. Drug allergy		
a) Penicillin	2	0.6
b) Sulfa drug	2	0.6
c) Naproxen	1	0.3
d) Carbamazepine	1	0.3

8.9 DETAILS ABOUT CURRENT ADR ADMISSION

A total of 71 adverse drug events were noted in this current hospitalisation (out of which 17 patients admitted with some other problem were found to have these additional drug related side effects). Out of these 71 events, 5 were purely because of essential drug omission and the rest were due to inappropriate prescribing. Of the 71 ADEs, 33 events were dyselectrolytemias, and hyponatremia is the major contributor.

Table 27 Details of past adverse drug events

ADE s due to inappropriate drugs	Counts	Percentage
1. Dyselectrolytemia		
a) Dehydrational hyponatremeia		
i. Loop Diuretic related hyponatremia	7`	10
ii. Thiazide related hyponatermia	4	5.7
b) SIADH with hyponatremia		
i. Antipsychotic related	2	2.9
ii. Amitriptyline	1	1.4
iii. SSRI	2	2.9
iv. Carbamazepine related	1	1.4
c) Hyperkalemia		
i. ACEI related	7	10
ii. Spironolactone related	1	1.4
d) Hypokalemia – Lasix related	5	7.1
e) Hypomagnesiumia - Lasix related	2	2.9
f) Hypercalcemia – multiple arachitol inj related	1	1.4
2. Hypoglycaemia		
a) Actrapid	1	1.4
b) Glipizide	1	1.4
3. Acute kidney injury		
a) Spironolactone	1	1.4

	b) Inj Diclofenac, Gentamycin	1	1.4
4.	Stage 5 Chronic kidney disease - NSAID related CIN	4	5.7
5.	Metformin related GI intolerance	1	1.4
6.	Subacute intestinal obstruction		
	a) Amitriptyline	1	1.4
	b) Tramadol, cinnarizine and escitalopram	1	1.4
7.	Pedal edema		
	a) Amlodipine	1	1.4
	b) Cilnidipine	1	1.4
	c) Moxonidine	1	1.4
8.	Prazosin related postural hypotension	1	1.4
9.	a) Sotalol related symptomatic bradycardia	1	1.4
	b) Symptomatic 1st degree heart block to atenolol	1	1.4
	c) Asymptomatic trifasicular block secondary to carvedilol	2	2.9
	d) Asymptomatic trifasicular block secondary to metoprolol	1	1.4
10.	Alprax related fall	1	1.4
11.	Delirium		
	a) Trihexyphenidyl	1	1.4
	b) Ropinirole	1	1.4
	c) Pregabalin	1	1.4
12.	Ropinirole related visual hallucination	1	1.4
13.	BOO to tolterodine	1	1.4
14.	Inappropriate anticoagulation		
	a) Overanticoagulation causing Intracranial bleed	1	1.4
	b) Inadequate anticoagulation		
	i. Stroke due to inadequate anticoagulation	2	2.9
	ii. Pulmonary embolism	2	2.9
	iii. ACS in 2* APLA	1	1.4
15.	Respiratory arrest secondary to midazolam	1	1.4

8.10 ADE s due to drug omission

16.	Not on bisphosphanates after a fragility fracture , resulting in another fracture	2	2.9
17.	Not on aspirin and statin after CAD, and sustained a stroke	1	1.4
18.	Not an antifailure drugs presented with CCF	1	1.4
19.	Not compliant to immunosuppressant in ANCA vasculitis , resulting in disease flare	1	1.4

8.11 Risk factor assessment – with univariate and multivariate analysis

We have also studied the probable risk factors for potentially inappropriate drug use. The factors were classified as demographic factors, performance factors, comorbidity status, pharmacokinetic factors and treatment factors. We have used both univariate and multivariate analysis to study the associations of these factors with inappropriate medication prescribing including renally inappropriate drugs, ADEs, and polypharmacy use. We have used Pearson chi square equation for doing univariate analysis. The categorical variables with p value < 0.2 were included in multivariate analysis and logistic regression was done to see the adjusted effect to identify independent risk factors for PIM use, Ade's occurrence and polypharmacy. Multivariate analysis could not be done for renally inappropriate drugs because of the small numbers.

8.12 Univariate analysis - summary of risk factor predisposition to PIM use.

Age was found to be an important risk factor. Patients with age 70 to 80 years when compared with young elderly population i.e. 60 to 70 years, had 1.78 times at higher risk for PIM usage (p=0.035, CI 0.13 – 1.25) and age more than 80 years had 3 times higher risk for PIM usage when compared with young elderly. (p= 0.012, CI 1.28 – 7.19). There was no increased risk observed with gender, educational and socio economic status. Patients living alone were not found to be at increased risk for PIM use in our study, and in fact it was shown to be beneficial having a preventive effect, (OR 0.41, p=0.116, CI 0.13 – 1.25), but this has to be interpreted with caution because of the fact that patient living alone was seen in very small numbers (0.15%) in our study population.

Patients with depression (assessed with GDS) were found to have an increased risk of PIM usage. With GDS > 5, there was a 3 fold increased risk of PIM use (p=0.003, CI 1.45 – 6.13) .People having disturbed sleep which warrants then to use any of the sedative at some point

in life had 3 fold of increased risk of using a PIM (p= <0.001, CI 1.72 – 5.61). There was an increasing trend for PIM use in people with lesser functional status and cognitive impairment.

The greater the comorbidity score, the higher was the risk for PIM. Patients with Charlson index > 3, had 2.74 times odds of getting exposed to PIM (p = 0.020, CI 1.17 – 6.42). Similarly patients using more drugs were exposed to PIM use. There was not much difference for patients using more than 5 drugs (OR 1.47, p=0.138, CI 0.88 – 2.43), but patients using more than 10 drugs had a greater risk for PIM usage (OR 1.59, p=0.008, CI 1.13 – 2.24).

There was no difference with pharmacokinetic factors even in patients having reduced creatinine clearance (OR 1.21, p=0.495, CI 0.70 – 2.08).

As expected, patients who were treated by more than 2 doctors had an additional risk for PIM use. (OR 2.39, p=0.015, CI 1.19 – 4.81). Interestingly patients treated by non-physicians or non-geriatricians had a greater risk for getting a PIM, especially with psychiatrist and surgeons. (OR 2.3, p=0.007, CI 1.27 – 4.49). There was an increasing trend for PIM for people who were not complaint to drugs and who could not take their own medicines and required assistance.

Table 28 Univariate analysis – comparing clinical dependent variables with PIM use

Clinical variables	Odds ratio	Confidence interval	*p* value
1. <u>Demographic factors:</u>			
a) Age.			
(60 – 70 as ref)			
• 71 – 80 yrs	1.78	1.04 – 3.04	0.035*
• Above 80 yrs	3.03	1.28 – 7.19	0.012*
b) Gender			
(Male as ref)			
• Female	0.96	0.58 – 1.60	0.891
c) Current living status			
(Living with spouse /child as ref)			
• living alone	0.41	0.13 – 1.25	0.116
d) Educational status			
(Post graduates as ref)			
• Illiterate	0.61	0.18 – 2.05	0.425
• Schooling / diploma	0.75	0.23 – 2.49	0.642
e) Economic status (kuppusamy scale)			
(Middle class as ref)			
• Upper class	1.23	0.71 – 2.13	0.468
• Lower class	0.93	0.36 – 2.39	0.880
2. <u>Performance status:</u>			
a) Dependency status			
Completely Independent as ref)			
• Partially dependent with barthrel index > 10 /20	0.99	0.54 – 1.84	0.987
• Partially dependent with barthrel index < 10 /20	1.68	0.65 – 4.35	0.286
• Completely dependent	1.27	0.31 – 5.15	0.743
b) Functional status			
(Fully functional as ref)			
• Impaired	2.55	0.92 – 7.06	0.072
• Non functional	4.47	0.94 – 21.29	0.060
c) Cognitive status			
(Normal cognition as ref)			
• Minicog > 1	1.58	0.69 – 3.61	0.274
• Minicog ≤ 1	1.51	0.55 – 4.13	0.420
d) Mood status – depression			

(No depression as ref)			
• GDS ≤ 3			
• GDS > 3	1.50	0.47 – 4.74	0.492
e) Sleeping status	3.00	1.45 – 6.13	0.003*
(Normal sleep as ref)			
• Insomnia			
f) Visual abilities	3.11	1.72 – 5.61	<0.001**
(Cataract with IOL (ref)			
• Cataract with no IOL			
g) Hearing abilities	0.54	0.31 – 0.95	0.033*
• Hearing impairment with aid (ref)			
• Hearing impairment with no aid	1.35	0.75 – 2.42	0.321
3. <u>Comorbidity status</u>			
(with no disease as reference)			
a) Diabetes mellitus	1.15	0.70 – 1.91	0.577
b) Coronary artery disease	1.15	0.62 – 2.12	0.657
c) Chronic kidney disease	1.36	0.78 – 2.37	0.279
d) Cerebrovascular accident	1.18	0.60 – 2.31	0.629
e) Parkinsonian disorders	1.24	0.58 – 2.65	0.585
f) Malignancy	0.61	0.25 – 1.49	0.277
g) Charlson comorbidity index (≤ 3 as ref)			
• 4 – 6	2.74	1.17 – 6.42	0.020*
• > 6	2.16	0.91 – 5.11	0.080
a) <u>Pharmacokinetic factors</u>			
b) BMI (18.5 – 24.9 as ref)			
• < 18.5	0.56	0.19 – 1.66	0.298
• 25 – 30	0.47	0.25 – 0.89	0.020*
• > 30	0.91	0.44 – 1.87	0.803
c) Crcl (abbr MDRD ≥ 60 ref)			
• < 60	1.21	0.70 – 2.08	0.495
d) Albumin (≥ 2.5 as ref)			
• < 2.5	0.88	0.35 – 2.22	0.778
e) Swallowing impairment			
(normal swallowing as ref)	1.23	0.52 – 2.92	0.642

4. Treatment factors			
a) Polypharmacy (> 5 drugs)	1.47	0.88 – 2.43	0.138
b) Excessive polypharmacy(> 10 drugs)	1.59	1.13 – 2.24	0.008*
c) Treating doctors (Physician as ref)			
• Geriatrician	1.14	0.43 – 3.01	0.791
• Others	2.39	1.27 – 4.49	0.007*
d) Number of treating doctors (1 doctors as ref)			
• 2 doctors	1.35	0.77 – 2.38	0.298
• > 2 doctors	2.39	1.19 – 4.81	0.015*
e) Infrequent health check up (minimum of 6 monthly check up as ref)	1.14	0.67 – 1.94	0.628
f) Cost of treatment (< 500 rupees as ref)			
• 500 – 1000 rupees / month	1.04	0.57 – 1.87	0.907
• > 1000 rupees / month	1.81	0.96 – 3.42	0.069
g) Self medication use	0.57	0.12 – 2.78	0.482
h) Over The Counter medication use	1.56	0.63 – 3.85	0.332
i) Ignorance about the treatment	0.75	0.21 – 2.74	0.669
j) Non compliance to treatment	1.87	0.94 – 3.70	0.076
k) Assisted drug administration	1.54	0.91 – 2.63	0.110

*p value < 0.05, ** p < 0.001

8.13 Multivariate analysis – Independent risk factors for PIM use

In multivariate analysis, age, functional status and depression were found to be independent risk factors for PIM usage.

When compared with young elderly, 70 to 80 year old people had odds of 2.41 (p=0.027, CI 1.10 – 5.25) and above 80 year old had odds of 3.95 (p=0.022, CI 1.22 – 12.77) to getting exposed to PIM. Patients with poor functional status had 11 times greater risk (OR 11.53, p=0.028, CI 1.31 – 101.41) for PIM use and people who were depressed had 3 times higher risk (OR 3.05, p=0.023, CI 0.16 – 7.99) for PIM use.

However , comorbidity index, polypharmacy , number of treating physicians which were found to be significant risk factors for PIM usage in univariate analysis, were not found to be independent risk factors when adjusted in multivariate analysis, but they showed a positive trend in causing PIM usage. There was an increasing trend for PIM use in people who are dependent for ADLs, cognitively impaired and people who are using Over The Counter medications.

Table 29 Multivariate analysis – comparing clinical variables with PIM use

Clinical variables	Odds ratio	Std error	Confidence interval	*p* value
1. Demographic factors:				
a) Age (60-70 as ref)				
• 70 – 80 yrs	2.41	0.96	1.10 – 5.25	0.027*
• Above 80 yrs	3.95	2.36	1.22 – 12.77	0.022*
b) Gender (male as ref)				
• Female	0.92	0.34	0.45 – 1.88	0.814
c) Economic status (kuppusamy scale) (middle class as ref)				
• Upper class	0.71	0.30		0.412
• Lower class	1.58	1.20	0.32 – 1.60	0.550
			0.35 – 7.01	
2. Performance status:				
a) Dependency status (independent as ref)				
• Partial dependent with barthrel index ≥ 10	0.82	0.37	0.34 – 1.98	0.656
• Partial dependent with barthrel index < 10	2.88	2.11	0.68 – 12.13	0.150
• Completely dependent	1.81	1.93	0.23 – 14.52	0.574
b) Functional status: (fully functional as ref)	2.56	1.76		0.170
• Impaired	11.53	12.79	0.67 – 9.83	0.028*
• Non functional			1.31 – 101.41	
c) Cognitive status (normal cognition as ref)	1.32	0.87		0.677
	0.61	0.52		0.565

• Minicog > 1				
• Minicog ≤ 1			0.36 – 4.80	
d) Mood status	0.93	0.70	0.12 – 3.22	0.919
(no depression as ref)	3.05	1.50		0.023*
• GDS ≤ 3				
• GDS > 3			0.21 – 4.11	
			0.16 – 7.99	
3. <u>Comorbidity status</u> (no disease as ref)				
a) Diabetes mellitus	0.96	0.42	0.41 – 2.26	0.922
b) Coronary artery disease	1.26	0.57	0.52 – 3.07	0.611
c) Cerebrovascular accident	0.69	0.37	0.24 – 1.96	0.488
d) Parkinsonian disorder	0.90	0.53	0.28 – 2.88	0.863
e) Charlson comorbidity index (≤ 3 as ref)	1.19	0.72	0.36 – 3.93	0.775
• 4-6	0.30	0.23	0.07 – 0.32	0.112
• > 6				
4. <u>Pharmacokinetic factors</u>				
BMI (18.5 – 24.9 as ref)				
• < 18.5	2.50	2.31	0.41 –	0.320
• 25 – 30	0.92	0.91	15.24	0.935
• > 30	1.88	1.97	0.13 – 6.41	0.547
			0.24 – 14.61	
5. <u>Treatment factors:</u>				
a) Polypharmacy (> 5 drugs)	0.92	0.44	0.36 – 2.35	0.865
b) Excessive polypharmacy (> 10 drugs)	1.70	0.91	0.59 – 4.86	0.322
c) Treating doctors (physicians as ref)				
• Geriatrician	0.73	0.52	0.18 – 2.96	0.654
• Others	1.94	1.42	0.46 – 8.11	0.366
d) Number of treating doctors (1 doctor as ref)				
• 2 doctors	0.60	0.44	0.14 – 2.50	0.482
• > 2 doctors	0.95	0.79	0.19 – 4.84	0.950
e) Infrequent health check up	1.81	0.72	0.83 – 3.95	0.138
(minimum of 6 monthly check up as ref)				
f) Cost of treatment (< 500 rupees per month as ref)	1.86	0.66	0.93 – 3.72	0.078
	2.76	1.82	0.76 – 10.08	0.123
g) Over The Counter medication use				

<u>*p value < 0.05</u>

8.14 Univariate analysis - summary of risk factor predisposition to the use of renally inappropriate drugs.

In univariate analysis, we found that people who were illiterate (OR 5.41, p=0.010, CI 0.51 – 19.48) and from low socioeconomic status (OR 4.39, p=0.025, CI 1.21 – 15.98) were more at risk for getting exposed to renally inappropriate drugs.

People who used self-medication (OR 29.55, p=<0.001, CI 6.95 – 125.53) and OTC (13.89, p=<0.001, CI 4.51 – 42.78) were at greater risk for getting exposed to renally inappropriate drug , because of the very fact that a commonly dispensed drug over the counters is NSAIDs in developing countries like India, which are directly nephrotoxic.

The patients having underlying CKD (OR 9.98, p= <0.001, CI 3.11 – 32.08) or having reduced creatinine clearance (OR 12.74, p<0.001, CI 3.52 – 46.08)were at more than10 times higher risk of getting exposed to renally inapproiate drugs especially those drugs which require dose adjustments. This is mainly because of failure to recognise estimated creatinine clearance in our people by the treating physicians, who were going only by creatinine values. This can come down only if treating doctors understands renal aging physiology.

Female showed an increasing trend of getting exposed to renally inappropriate drugs (OR 1.98, p=0.189, CI 0.71 – 5.48). This can be explained by the fact , that degenerative joint disease is present in 77.9% of female when compared with 50.5% of males(Pearson chi square, p<0.001) and NSAID abuse was reported in17.7% of our females in study population when compared with only 4.8% of males(Pearson chi square, p<0.001). Totally we had 8 patients with stage 5 CKD and NSAID abuse was found to be the culprit in causing stage 5 CKD in 2 of our patient (25%).

Patients with low albumin (< 2, 5) had an increasing trend of getting exposed to renally inappropriate drugs (OR 2.66, p=0.154, CI 0.69 – 10.23). Two reasons we could attribute, one is low protein binding capacity increasing the serum free drug concentration eliciting renal injury and the other is morbidly sick patients either acute or chronic having a higher chance of getting exposed to more renally inappropriate drugs like antibiotics, antifungals, NSAIDs and even radio contrast agents while exposing them to higher diagnostic techniques. Multivariate analysis could not be done because of small numbers (0.06%) being exposed to renally inappropriate drugs

Table 30 Univariate analysis – comparing clinical variables with renally inapporpiate drug use

Clinical variables	Odds ratio	Confidence interval	*p* value
1. Demographic factors:			
a) Age (60 – 70 yrs as ref)			
• 71 – 80 yrs	0.47	0.15 – 1.50	0.204
b) Gender (males as ref)			
• Female	1.98	0.71 – 5.48	0.189
c) Current living status (living with spouse/children as ref)			
• living alone	0.30	0.06 – 1.51	0.145
d) Educational status (literate as ref)			
• Illiterate	5.41	0.51 – 19.48	0.010*
e) Economic status (kuppusamy scale) (middle class as ref)			
• Upper class	1.07	0.31 – 3.66	0.914
• Lower class	4.39	1.21 – 15.98	0.025*
2. Performance status:			
a) Dependency status (fully independent as ref)			
• Partially dependent with barthrel index > 10 /20	0.74	0.18 –3.06	0.683
• Partially dependent with barthrel index < 10 /20	0.62	0.54 –7.11	0.702

b) Functional status (normal function as ref)			
• Impaired	0.21	0.07 – 0.70	0.011*
• Non functional	0.61	0.04 –8.75	0.719
c) Mood status – depression (no depression as ref)			
• GDS ≤ 3	1.29	0.16 –10.66	0.812
• GDS > 3	0.44	0.06 – 3.47	0.438
d) Sleeping status (normal sleep as ref)			
• Insomnia	0.52	0.69 – 2.35	0.394
e) Visual abilities (cataract with IOL as ref)			
• Cataract with no IOL	1.31	0.35 – 4.92	0.686
f) Hearing abilities(HOH with aid as ref)			
• Hearing impairment with no aid	0.24	0.30 – 1.84	0.168
3. <u>Comorbidity status</u> (no disease as ref)			
a) Diabetes mellitus	0.46	0.16 – 1.29	0.139
b) Coronary artery disease	0.92	0.25 – 3.34	0.898
c) Chronic kidney disease	9.98	3.11 – 32.08	<0.001**
d) Cerebrovascular accident	0.34	0.04 – 2.66	0.306
e) Malignancy	0.56	0.07– 4.42	0.584
f) Charlson comorbidity index (≤ 3 as ref)			
• 4 – 6	1.44	0.29 – 7.05	0.654
• > 6	1.23	0.22 – 5.82	0.885
4. <u>Pharmacokinetic factors</u>			
a) BMI (18.5 – 24.9 as ref)			
• < 18.5	1.74	0.35 – 8.73	0.502
• 25 – 30	0.80	0.24 – 2.68	0.716
• > 30	0.37	0.05 – 3.00	0.352
b) Crcl (abbr MDRD > 60 as ref)			
• < 60	12.74	3.52 – 46.08	<0.001**
c) Albumin (> 2.5 as ref)			
• < 2.5	2.66	0.69 – 10.23	0.154
d) Swallowing status (normal swallowing as ref)	0.70	0.09 – 5.53	0.734
5. <u>Treatment factors</u>			
a) Polypharmacy (> 5 drugs)	0.37	0.12 – 1.09	0.070
b) Excessive polypharmacy(> 10 drugs)	0.55	0.25 – 1.24	0.149
c) Treating doctors (physicians as ref)			

• Others	0.52	0.19 – 1.46	0.213
d) Number of treating doctors (1 doc as ref)			
• 2 doctors	0.60	0.21 – 1.73	0.343
• > 2 doctors	0.24	0.03 – 1.92	0.177
e) Infrequent health check up (minimum of 6 monthly check up as ref)	2.30	0.83 – 6.34	0.108
f) Cost of treatment (<500 rupees /mon as ref)			
• 500 – 1000 rupees / month	0.26	0.06 – 1.20	0.084
• > 1000 rupees / month	0.38	0.08 – 1.79	0.222
g) Self medication use	29.55	6.95 – 125.53	<0.001**
h) Over The Counter medication use	13.89	4.51 – 42.78	<0.001**
i) Non compliance to treatment	1.44	0.39 – 5.31	0.582
j) Drug administration – assisted	0.31	0.69 – 1.40	0.129

* is p<0.05, ** is p <0.001

8.15 Univariate analysis - summary of risk factor predisposition to the occurrence of ADE

In univariate analysis, we found that people who were depressed had a significantly higher risk of developing an ADE. (OR 2.71, p=0.008, CI 1.30 – 5.65). The reason was identified as the use of multiple inappropriate drugs like benzodiazepines (Pearson chi square p0.013) , antidepressants with high anticholinergic activity like amitriptyline(Pearson chi square p<0.001), etc. and even antipsychotics (Pearson chi square p0.002) ,which can all precipitate delirium , produce falls and worsens constipation.

Similarly patients using OTC drugs had a trend to be more prone for ADEs (2.12, p=0.112, CI 0.84 – 5.37). The commonest reason we could identify was PRN usage of sedatives, using codeine based cough syrups, and the more common NSAIDs for pain relief, which can all precipitate ADEs.

Patients with chronic kidney disease or with creatinine clearance < 60 were at higher risk (OR1.96, p=0.026, CI 1.08 – 3.56), the reason was attributed to using OHAs in patient with CRF leading to more hypoglycaemic episodes , incurring dyselectrolytemias, esp.

hyperkalaemia with ACEIs in the setting of renal failure. Out of the total 5 glibenclamide users, 3 had creatinine clearance less than 60 which when cross tabulated showed a significant higher proportion of use of long acting sulphonyl user in renal failure (Pearson chi square $p<0.001$), thus increasing the risk of hypoglycaemia related hospitalisation.

Patients with CAD and CVAs had a significant association with the occurrence of an ADE. The reason was attributed to the usage of multiple drugs in both the settings and especially usage of diuretics which can cause many dyselectrolytemias. Out of 56 patients having CAD, 80% were using more than 5 drugs and 34% were using more than 10 drugs, which is definitely higher when compared with the total population of 280 patients.

There was an increasing trend with DM, people having higher comorbidity index > 6, usage of excessive polypharmacy with the occurrence of ADEs. However there was no significant association found between patients with parkinsonian disorder and malignancy and the occurrence of ADEs.Similarly, patients who are completely dependent had an increasing trend towards developing ADEs, but they were not statistically significant. We could not find any statistical significant associations between cognitively impaired patient and occurrence of ADEs.

Interestingly patient belonging to the upper class were found to have lower incidence of ADEs (OR0.51, $p =0.049$, CI 0.26 – 0.99), this can be explained by the fact, that their follow up is very much adequate and they are monitored for the electrolytes, INR, Sugars periodically and it is complemented by the fact that people following infrequently has a higher risk for developing ADEs. It is understood that the majority of ADE can be prevented by a simple measure of adequate monitoring and health visits to a doctor. Patient living alone showed low OR, which could not be interpreted because of small study group of 14 patients.

Table 31 Univariate analysis – comparing clinical dependent variables with ADEs

Clinical variables	Odds ratio	Confidence interval	*p* value
1. Demographic factors:			
a) Age (60 -70 yrs as ref)			
• 71 – 80 yrs	1.03	0.58 – 1.3	0.930
• Above 80 yrs	0.26	0.59 – 1.56	0.077
b) Gender (male as ref)			
• Female	0.96	0.55 – 1.69	0.887
c) Current living status (living with spouse/children as ref)	0.24	0.08 – 0.75	0.014*
• living alone			
d) Educational status (post graduates as ref)			
• Illiterate	1.00	0.25 – 3.93	1.000
• Schooling / diploma	0.86	0.22 – 3.39	0.835
e) Economic status (kuppusamy scale) (middle class as ref)			
• Upper class	0.51	0.26 – 0.99	0.049*
• Lower class	0.73	0.26 – 2.09	0.564
2. Performance status:			
a) Dependency status (independent as ref)			
• Partially dependent with barthrel index > 10 /20	1.05	0.51 – 2.15	0.892
• Partially dependent with barthrel index < 10 /20	1.44	0.48 – 4.27	0.513
• Completely dependent	2.67	0.58 – 12.36	0.208
b) Functional status (normal function as ref)			
• Impaired	0.45	0.19 – 1.05	0.066
• Non functional	0.52	0.11 – 2.49	0.411
c) Cognitive status (normal cognition as ref)			
• Minicog > 1	0.57	0.19 – 1.73	0.321
• Minicog ≤ 1	1.30	0.44 – 3.87	0.627
d) Mood status – depression (no depression as ref)			
• GDS ≤ 3	1.14	0.30 – 4.30	0.849
	2.71	1.30 – 5.65	0.008*

• GDS > 3			
e) Sleeping status (normal sleep as ref)	1.41	0.74 – 2.70	0.295
• Insomnia			
f) Visual abilities (cataract with IOL as ref)	0.99	0.52 – 1.88	0.965
• Cataract with no IOL			
g) Hearing abilities (HOH with aid as ref)	0.83	0.42 – 1.65	0.599
• Hearing impairment with no aid			
3. <u>Comorbidity status</u> (no disease as ref)			
a) Diabetes mellitus	1.69	0.95 – 2.99	0.074
b) Coronary artery disease	2.46	1.30 – 4.63	0.006*
c) Chronic kidney disease	1.96	1.08 – 3.56	0.026*
d) Cerebrovascular accident	3.04	1.55 – 5.98	0.001*
e) Parkinsonian disorders	1.09	0.46 – 2.55	0.849
f) Malignancy	0.51	0.17 – 1.52	0.226
g) Charlson comorbidity index (≤3 as ref)			
• 4 – 6	1.46	0.59 – 3.65	0.416
• > 6	2.01	0.81 – 4.97	0.132
4. <u>Pharmacokinetic factors</u>			
a) BMI			
• < 18.5	1.45	0.48 – 4.38	0.505
• 25 – 30	1.63	0.85 – 3.10	0.138
• > 30	1.49	0.67 – 3.34	0.329
b) Crcl (abbr MDRD> 60 as ref)			
• < 60	1.80	1.00 – 3.22	0.050*
c) Albumin (> 2.5 as ref)			
• < 2.5	2.36	0.96 – 5.78	0.061
d) Swallowing status (normal swallowing as ref)	0.62	0.20 – 1.89	0.403
5. <u>Treatment factors</u>			
a) Polypharmacy (> 5 drugs)	1.33	0.76 – 2.32	0.321
b) Excessive polypharmacy(> 10 drugs)	1.30	0.89 – 1.89	0.169
c) Treating doctors (physician as ref)			
• Geriatrician	0.98	0.38 – 2.55	0.963
• Others	0.93	0.49 – 1.77	0.832
d) Number of treating doctors (1 doc as ref)			
• 2 doctors	1.05	0.57 – 1.93	0.866

• > 2 doctors	0.95	0.42 – 2.11	0.893
e) Infrequent health check up (minimum of 6 monthly check up as ref)	1.45	0.81 – 2.59	0.206
f) Cost of treatment (< 500 rupees /mon as ref)			
• 500 – 1000 rupees / month	1.17	0.63 – 2.21	0.626
• > 1000 rupees / month	1.05	0.51 – 2.17	0.895
g) Self medication use	1.64	0.40 – 6.76	0.491
h) Over The Counter medication use	2.12	0.84 – 5.37	0.112
i) Non compliance to treatment	1.30	0.61 – 2.78	0.499
j) Drug administration - assisted	0.76	0.41 – 1.41	0.382

* is $p<0.05$

8.16 Multivariate analysis - summary of risk factor predisposition to the occurrence of ADE

In multivariate analysis, the factors identified as independent risk factors for ADEs were patient having CAD, CVA or depression, and using OTC medication. However CKD which showed significant univariate associations with ADEs failed to be an independent risk factor when adjusted (OR 2.34, p=501, CI 0.20 – 27.78).

Charlson comorbidity index, functioning and cognitive status were not found to be associated with ADE occurrence. There was increased risk of ADE with age, dependency status, hypoalbuminemic status, having diabetes, using excessive polypharmacy, and doing infrequent health check up to cause ADE. The point which we liked to emphasize is that, infrequent health check and inadequate monitoring increases the risk of ADEs and mortality, which can be easily avoided with regular health visit and appropriate timely monitoring.

Table 32 multivariate analysis – comparing clinical variables with ADE

Clinical variables	Odds ratio	Std error	Confidence interval	*p* value
1. Demographic factors:				
a) Age (60 – 70 yrs as ref)				
• 70 – 80 yrs	2.07	0.90	0.88 – 4.88	0.095
• Above 80 yrs	0.18	0.21	0.02 – 1.75	0.138
b) Gender (male as ref)				
• Female	0.85	0.35	0.37 – 1.98	0.706
c) Economic status (kuppusamy scale) (middle class as ref)				
• Upper class	0.45	0.23	0.17 – 1.20	0.111
• Lower class	0.28	0.24	0.05 – 1.51	0.140
2. Performance status:				
a) Dependency status (independent as ref)				
• Partial dependent with barthrel index ≥ 10	0.92	0.49	0.32 – 2.63	0.874
• Partial dependent with barthrel index < 10	0.96	0.76	0.21 – 4.48	0.962
• Completely dependent	1.61	1.95	0.15 – 17.17	0.691
b) Functional status: (normal functioning as ref)				
• Impaired	0.51	0.31	0.16 – 1.65	0.261
• Non functional	0.60	0.68	0.06 – 5.58	0.651
c) Cognitive status (normal cognition as ref)				
• Minicog > 1	0.38	0.31	0.08 – 1.85	0.231
• Minicog ≤ 1	1.12	0.96	0.21 – 6.02	0.894
d) Mood status – depression (no depression as ref)				
• GDS ≤ 3	1.07	1.05	0.16 – 7.32	0.942
• GDS > 3	5.30	2.86	1.84 – 15.25	0.002*
3. Comorbidity status (no disease as ref)				
a) Diabetes mellitus	1.48	0.75	0.54 – 4.02	0.442
b) Coronary artery disease	5.22	2.69	1.90 – 14.35	0.001*
c) Chronic kidney disease	2.34	2.95	0.20 – 27.78	0.501
d) Cerebrovascular accident	3.20	1.74	1.10 – 9.31	0.033*

e) Parkinsonian disorder	1.53	1.03	0.41 – 5.75	0.531
f) Charlson comorbidity index (≤ 3 as ref)				
• 4-6	0.94	0.63	0.25 – 3.52	0.925
• > 6	0.58	0.49	0.11 – 3.04	0.516
4. Pharmacokinetic factors				
a) BMI (18.5 – 24.9 as ref)				
• < 18.5	0.36	0.30	0.07 – 1.88	0.224
• 25 – 30	0.41	0.38	0.07 – 2.57	0.340
• > 30	0.84	0.86	0.12 – 6.15	0.867
b) Crcl (abbr MDRD > 60 as ref)				
• < 60	0.93	1.16	0.08 – 10.76	0.956
c) Albumin (> 2.5 as ref)				
• < 2.5	2.68	2.04	0.61 – 11.87	0.194
5. Treatment factors:				
a) Polypharmacy (> 5 drugs)	0.87	0.48	0.30 – 2.57	0.805
b) Excessive polypharmacy (> 10 drugs)	1.31	0.86	0.37 – 4.72	0.677
c) Treating doctors (physician as ref)				
• Geriatrician	2.28	1.66	0.55 – 9.48	0.256
• Others	0.32	0.27	0.06 – 1.68	0.180
d) Number of treating doctors (1 doc as ref)				
• 2 doctors	2.88	2.41	0.56 – 14.84	0.207
• > 2 doctors	1.36	1.40	0.18 – 10.24	0.766
e) Infrequent health check up (atleast 6 monthly visit as ref)	1.87	0.84	0.78 – 4.50	0.160
f) Cost of treatment (< 500 rupees /mon as ref)	0.85	0.35	0.38 – 1.89	0.695
g) Over The Counter medication use	5.27	3.98	1.20 – 23.17	0.028*
h) Non compliance to treatment	0.94	0.53	0.31 – 2.83	0.916

* is $p<0.05$

8.17 Univariate analysis - summary of risk factor predisposition to polypharmacy

As expected, people with high Charlson comorbidity index were found to have a significant association with polypharmacy. With an index of more than 3, there is 1.88 odds (p=0.091, CI0.90 – 3.90) of getting exposed to polypharmacy no statistically significant, which gets doubled if the index is > 6. (OR 4.55, p=<0.001, CI 2.15 – 9.62).

Interestingly, people with diabetes have a 4.53 times (p=<0.001, CI 2.73 – 7.50) greater risk of getting exposed to polypharmacy. The reason which we could attribute was coexistent hypertension and dyslipidemic state in most of our patient. Similarly in patients with CAD (OR 4.55, p=<0.001, CI 2.24 – 9.26) and CVA (OR 2.62, p=0.008, CI 1.29 – 5.34), exposure to polypharmacy was higher.

Obese individuals are exposed to polypharmacy more when compared with normal BMI individuals. The reason was identified as coexistent multiple vascular risk factors like DM, HTN, DL, CAD and CVAs in obese individual. And complementarily, low BMI individuals have lesser risk for polypharmacy, and this is not only because of absence of vascular risk factors but these people mainly belong to the lower socioeconomic groups (p=0.076).

A person treated by geriatrician and doctors other than physicians had a greater risk. But this is contradictory very much because of the fact that geriatrician are better with drugs especially in the elderly. But what we found was geriatricians were treating a higher proportion of patients with higher comorbid index, diabetics, CAD and CVA.

Patients seeking more than 2 doctors were at greater risk (OR 4.35, p=<0.001, CI 2.11 – 8.97). The main reason found was communication gap between doctors, which results in drug duplication and frequent change of drugs resulting in patient confusion as to what drug to actually use.

As expected, patients who required someone's help had increased risk for getting exposed to multiple drugs (OR 2.22, p=0.004, CI 1.30 – 3.81), the reason being high comorbid index, and coexistent functional, and cognitive impairment.

People who are depressed are also at higher risk for exposure to more drugs and this is because of the high comorbid status of these patients, and usage of CAM medicines. The reasons are multifactorial:

1. People with depression were found to have a higher proportions of demented people (p=0.002)
2. Most of the time they are treated by more than 2 doctors and the proportion of people with depression consulting more than 2 doctors is more than the total population. (p0.041).
3. And lastly, people with depression were found using some form of CAM very frequently more than the other patients with no depression.

All these factors contribute to the increased risk of polypharmacy in patients with depression. Similar risk was found in upper class people and in fact lower class people have a protective effect against polypharmacy. [Upper class, (OR 2.13, p=0.007, CI 1.27 – 3.70), lower class (OR 0.43, p 0.079 and CI 0.17 – 1.10)].There is significant risk seen with age, dependency, functional and cognitive status with exposure to polypharmacy.

Table 33 Univariate analysis – comparing clinical dependent variables with polypharmacy

Clinical variables	Odds ratio	Confidence interval	*p* value
1. **Demographic factors:**			
a) Age (60 – 70 yrs as ref)			
• 71 – 80 yrs	1.31	0.79 – 2.16	0.299
• Above 80 yrs	1.46	0.62 – 3.46	0.388
b) Gender (male as ref)			
• Female	1.53	0.94 – 2.48	0.085
c) Current living status (living with spouse/children as ref)			
• living alone	1.00	0.33 – 3.07	0.995
d) Educational status (post graduates as ref)			
• Illiterate	0.81	0.25 – 2.66	0.730
• Schooling / diploma	1.65	0.51 – 5.37	0.407
e) Economic status (kuppusamy scale) (middle class as ref)			
• Upper class	2.13	1.27 – 3.70	0.007*
• Lower class	0.43	0.17 – 1.10	0.079
2. Performance status:			
a) Dependency status (independent as ref)			
• Partially dependent with barthrel index > 10 /20	1.51	0.84 – 2.73	0.169
• Partially dependent with barthrel index < 10 /20	1.37	0.51 – 3.64	0.530
• Completely dependent	3.88	0.80 – 18.81	0.092
b) Functional status (normal function as ref)			
• Impaired	2.03	0.92 – 4.47	0.080
• Non functional	0.39	0.08 – 1.89	0.240
c) Cognitive status (normal cognition as ref)			
• Minicog > 1	1.22	0.54 – 2.77	0.632
• Minicog ≤ 1	1.64	0.59 – 4.59	0.343
d) Mood status – depression (no depression as ref)			
• GDS ≤ 3	5.55	1.20 – 25.58	0.028*
• GDS > 3	2.29	1.08 – 4.88	0.031*

e) Sleeping status (normal sleep as ref)			
• Insomnia	1.73	0.95 – 3.13	0.071
f) Visual abilities (cataract with IOL)			
• Cataract with no IOL	0.58	0.33 – 1.03	0.062
g) Hearing abilities (hearing impairment with no aid as ref)			
• Hearing impairment with no aid	1.92	1.06 – 3.46	0.031*
3. **Comorbidity status** (no disease as ref)			
a) Diabetes mellitus	4.53	2.73 – 7.50	<0.001**
b) Coronary artery disease	4.55	2.24 – 9.26	<0.001**
c) Chronic kidney disease	1.05	0.61 – 1.79	0.863
d) Cerebrovascular accident	2.62	1.29 – 5.34	0.008*
e) Parkinsonian disorders	1.11	0.53 – 2.33	0.780
f) Malignancy	1.06	0.49 – 2.29	0.887
g) Charlson comorbidity index (≤3 as ref)			
• 4-6	1.88	0.90 – 3.90	0.091
• >6	4.55	2.15 – 9.62	<0.001**
4. **Pharmacokinetic factors**			
a) BMI			
• < 18.5	0.33	0.11 – 0.96	0.042*
• 25 – 30	0.13	0.65 – 1.97	0.668
• > 30	2.22	1.05 – 4.70	0.037*
b) Crcl (abbr MDRD) < 60	0.92	0.55 – 1.55	0.762
c) Albumin < 2.5	0.40	0.16 – 0.99	0.048*
d) Swallowing status	1.21	0.52 – 2.84	0.651
5. **Treatment factors**			
a) Treating doctors (physician as ref)			
• Geriatrician	5.35	2.20 – 12.98	<0.001**
• Others	5.70	3.08 – 10.58	<0.001**
b) Number of treating doctors(1 doc as ref)			
• 2 doctors	3.70	2.15 – 6.38	<0.001**
• > 2 doctors	4.35	2.11 – 8.97	<0.001**
c) Infrequent health check up (minimum of 6 monthly check up as ref)	0.30	0.18 – 0.52	<0.001**

d) Cost of treatment (< 500 rupees/mon as ref)			
• 500 – 1000 rupees / month	20.10	9.81 – 41.14	<0.001**
• > 1000 rupees / month	42.00	15.25 – 115.62	<0.001**
e) Self medication use	0.67	0.18 – 2.57	0.564
f) Over The Counter medication use	0.40	0.16 – 1.02	0.056
g) Ignorance of the treatment	0.78	0.22 – 2.84	0.709
h) Non compliance to treatment	0.68	0.34 – 1.34	0.260
i) Drug administration - assisted	2.22	1.30 – 3.81	0.004*

* is p<0.05, ** is p <0.001

8.18 Multivariate analysis - summary of risk factor predisposition to polypharmacy

In multivariate analysis, age, cognitive impairment and dependency status along with having DM, CAD or CVA were found to be independent risk factors for polypharmacy. Surprisingly, when adjusted, higher comorbid index was not associated with polypharmacy. (OR 0.30, p=0.227, CI 0.04 – 2.09). The reason we found was that the proportion of people with diabetics and depression were more in the low comorbidity index group when compared with high index patients. When adjusted, there were no statistical associations found with treating physicians and the number of treating physicians with polypharmacy.

Table 34 Multivariate analysis – comparing clinical variables with polypharmacy use

Clinical variables	Odds ratio	Std error	Confidence interval	*p* value
1. Demographic factors:				
a) Age (60 – 70 yrs as ref)				
• 70 – 80 yrs	0.31	0.18	0.10 – 0.97	0.044*
• Above 80 yrs	0.55	0.67	0.07 – 4.69	0.587
b) Gender (male as ref)				
• Female	1.95	1.05	0.68 – 5.59	0.216
c) Economic status (kuppusamy scale) (middle class as ref)				
• Upper class	0.66	0.36	0.22 – 1.92	0.442
• Lower class	0.19	0.24	0.02 – 2.21	0.184
2. Performance status:				
a) Dependency status (independent as ref)				
• Partial dependent with barthrel index ≥ 10	2.08	1.44	0.53 – 8.10	0.292
• Partial dependent with barthrel index < 10	0.11	0.13	0.01 – 1.00	0.050*
• Completely dependent	0.28	0.47	0.01 – 7.60	0.448
b) Functional status: (normal function as ref)	3.11	2.33	0.72 – 13.48	0.130
• Impaired	1.87	2.89	0.09 – 38.61	0.685
• Non functional				
c) Cognitive status (normal cognition as ref)	8.64	8.07	1.39 – 53.86	0.021*
• Minicog > 1	2.49	3.05	0.23 – 27.35	0.455
• Minicog ≤ 1				
d) Mood status – depression (no depression as ref)	4.32	5.09	0.43 –43.46	0.214
• GDS ≤ 3	2.93	2.10	0.72 – 11.94	0.134
• GDS > 3				
3. Comorbidity status (no disease as ref)				
a) Diabetes mellitus	14.07	9.04	3.99 – 49.56	<0.001*
b) Coronary artery disease	4.89	3.67	1.13 – 21.27	*
c) Chronic kidney disease	2.24	3.75	0.08 – 59.86	0.034*
d) Cerebrovascular accident	6.01	5.87	0.89 – 40.76	0.631

e) Parkinsonian disorder	1.18	1.02	0.22 – 6.41	0.066
f) Charlson comorbidity index (≤ 3 as ref)				0.848
• 4-6	0.42	0.32	0.09 – 1.89	
• > 6	0.30	0.30	0.04 – 2.09	0.256
				0.227
4. Pharmacokinetic factors				
a) BMI (18.5 – 24.9 as ref)				
• < 18.5	2.48	3.56	0.15 – 41.47	0.528
• 25 – 30	1.46	2.19	0.08 – 27.34	0.799
• > 30	1.88	3.11	0.07 – 48.31	0.704
b) Crcl (abbr MDRD > 60 as ref)				
• < 60	0.45	0.76	0.02 – 12.03	0.635
c) Albumin (> 2.5 as ref)				
• < 2.5	1.02	1.01	0.15 – 7.05	0.983
5. Treatment factors:				
a) Treating doctors (physician as ref)				
• Geriatrician	5.66	4.79	1.08 – 29.73	1.08
• Others	2.20	2.64	0.21 – 23.25	0.21
b) Number of treating doctors (1 doc as ref)				
• 2 doctors	2.67	3.14	0.27 – 26.71	0.404
• > 2 doctors	0.64	0.84	0.05 – 8.41	0.735
c) Infrequent health check up (minimum 6 monthly check up as ref)	0.58	0.32	0.19 – 1.73	0.326
d) Cost of treatment (< 500 rupees/mon as ref)	17.06	8.34	6.54 – 44.49	<0.001*
e) Over The Counter medication use	2.40	2.13	0.42– 13.70	*
f) Non compliance to treatment	0.30	0.23	0.07 – 1.38	0.324
				0.123

* is p<0.05, ** is p <0.001

9. DISCUSSION

The proportion of the elderly is increasing with each decade all over the world and it is a known fact that the elderly and drugs are inseparable; the reason for this is the presence of underlying chronic disease conditions and the increased awareness and expectation of the population, including older people of remaining in good health. Unfortunately inappropriate prescribing is seen very commonly in our elderly people. This is not to be taken lightly as it is associated with potentially serious health outcomes and mortality. The fact that "all elderly are not old adults" has to be kept in mind before prescribing for any elderly person because of the physiological changes associated with ageing. Often, the elderly have plenty of comorbidities and complicated medical conditions which often warrant multiple drugs (polypharmacy), which can predispose to serious drug-drug/ drug – disease interaction and at times, can cost the life of elderly if not monitored closely

Many studies have shown that drug related morbidity and mortality is often preventable by simply avoiding the use of inappropriate drugs. Usage of these inappropriate drugs is the main risk factor associated with drug related ailments. There are many explicit criteria to screen for PIM use in the elderly, but amongst them Beers' criteria is the most evidence based and widely used criterion.

We had analysed a group of elderly people admitted in our ward, over a period of one and half years in a cross sectional manner and studied the appropriateness of their prescribed drugs using Beers' criteria. Our study was powered to 80% with an error fraction of 5% and the sample size was calculated assuming a prevalence of 22% based on data from other national studies(17)

9.1 Patient profile:

A total of 280 patients were recruited over a period of 18 months after fulfilling inclusion criteria. The mean ± SD age of the study population was 70 ± 3.9 years and most of them (72%) were between 60-70 years of age and only 2.95 were above the age of 80 years. The sample was primarily males (60%) and the majority of the people were either staying with their spouse or with children in more than 95% of cases. With respect to socioeconomic status, about 2/3 rd of population had got basic schooling and belonged to the middle class and less than 10% belonged to the lower socioeconomic class. This does not reflect our population considering that very few people are from the lower socioeconomic class, but this was not unexpected in a tertiary setup, where people who are educated, aware and belong to above average socioeconomic status seek medical help from tertiary center more often than lower class people, who usually find help from primary health centers. The median comorbidity burden which was calculated using Charlson comorbidity index in our study patients was 6, which also signifies more complex patients presenting to tertiary care centre. A detailed drug history was taken which screened all the drugs taken over the last 2 weeks, and the drugs were assessed for appropriateness according to Beers criteria and JAGS 2008 criteria. Essential drug omissions were assessed with START criteria(33), and other drug problem like drug /therapeutic duplications were also studied. The occurrence of ADEs of both current and past were also documented.

9.2 PREVALENCE OF PIM USE:

Out of these 280 patients, 276 patients (98.6%) were on regular medications. Out of these 276 people, a sum of 1790 drugs were prescribed with a mean consumption of 6.3 drugs per user, out of which 350 drugs (19.5% of total drugs prescribed) were considered inappropriate

according to Beers' criteria, which can be sub classified to 118 class 1 PIM, 188 class 2 PIM and 44 class 3 PIM.

Totally 93 patients out of 280 (33.2%) were found to be using atleast one 1 PIM. The majority of the population about 70% was found to be using one PIM and 21.3% were using 2 PIMs and very few, 7.5% were using more than 2 PIMs.

A systemic review published in BMC, 2011(11), estimated the prevalence of PIM to be 11.5 – 62.5%.But the higher incidence is due to the fact that it is a community based trial and it used many other explicit criteria other than Beers' criteria for identification of PIM. Many studies on PIM use in the hospitalised elderly using Beers' criteria, have documented a prevalence to in the range of 20-40%.But recently Vieira de lima et al(30), in a study done in Brazilian care homes, reported a much higher prevalence of 82% PIM users. Our finding are however consistent with many Indian studies (26), which have reported PIM usage in the range of 20-30% with the highest being 40%. The reason for the low prevalence in Indian studies when compared with the west and especially Brazilian data could be due to the difference in the study population and because the drugs mentioned in Beers' criteria were used more widely in the West when compared with Asian countries.

Amongst the inappropriate drugs / drug classes identified in our study, the major contributor was drugs with anticholinergic activity. A total of 47 drugs (39.9%) were identified using Beers' criteria which included 13.6% antimuscarinics, 11.9% antipsychotics, 8.5% TCAs and 5.9% first generation antihistaminics. This was followed by sedatives, with the majority being benzodiazepines, which comprised 22% of the class 1 PIM. Drugs with anticholinergic activity and sedatives together comprised more than 60% of PIM use.

The Brazilian study(30), documented antipsychotics to be the major contributor, followed by anxiolytics, analgesics and antidepressants. In the Brazilian study, only 1.1% of inappropriate prescribing was because of drug disease interaction, but this was not the case in our study, where we identified about 188 (53.7%) out of 350 PIM because of inappropriate drug – disease interaction (class 2 PIM). The commonest drug – disease interaction found in our study was use of major and minor tranquilizers in the setting of falls, delirium and dementia, which constitutes 28.7%, followed by drugs with anticholinergic activity in patients with delirium, dementia, constipation and symptomatic LUTS, which constituted 21.9% of drug – disease interactions.

Pandya et all reported inappropriately dosed spironolactone and digoxin as the major contributors (about 30%) to Class 2 PIMs and did not comment much about falls, dementia and delirium interactions. The main reason for this difference is that our study population was more aged, had a higher comorbid index and about 43% of our population was dependent either partially or completely and major drugs identified in PIM use were major and minor tranquilizers.

The other major drug disease interactions were mainly because of drugs with anticholinergic activity with constipation, symptomatic LUTS and dementia.

The next major class of drug contributing to PIM was identified as drugs affecting the cardiovascular system which constituted 21.2% of total class 1 PIM use. This mainly included inappropriately dosed spironolactone and digoxin and inappropriate use of alpha blockers, central alpha agonists and antiarrhythmics. There was no immediate release Nifedipine user found in our study, but the study done in a Malaysian nursing home, found immediate release nifedipine to be a major contributor to PIM use. The reason is probably increased awareness among the treating physicians regarding the side effect profile of

immediate release nifedipine since their college days. The study done in the Malaysian nursing home also found glibenclamide to be a major contributor to PIM use, but we found only 4 glibenclamide users. The reason could be the flurry of newer antidiabetics in the Indian market and the increased awareness of the side effect profile by our practitioners.

The Indian study done by Pandya et al(29), reported the use of mineral oil to be a major contributor to PIM use, whereas in our study only 2 patients were found to be using mineral oil regularly. The one reason for this mismatch was that our patients were not using mineral oil regularly and using it mainly on a PRN basis. Jhaveri et al(34), in an Indian study, done in 2010, reported that more than 50% of population was using Metoclopromide, but in our study we did not find even one regular user of metoclopromide.

On multivariate analysis, we found that increasing age, impaired functional status and underlying depression were significant independent risk factors for PIM usage. This was consistent with other studies(11)(30) .

In Brazilian study, polypharmacy was found to be an independent risk factor to PIM use. In our study, univariate analysis revealed significant associations with polypharmacy and excessive polypharmacy, but in multivariate analysis we could not find significant associations. A similar situation was taken in study by Pandiya et al. Just as in the Brazilian study(35), we had significant associations of comorbid index with PIM use in univariate analysis, but it was not significant when adjusted in multivariate analysis.

9.3 Prevalence of renally inappropriate drugs , according to Beers' criteria :

Only 16 patients (5.71%) were found to be using renally inappropriate drugs as defined by Beers' criteria and the most commonly used was NSAIDs. In the Brazilian study(35) and the study by Fick et al(36), NSAIDs was the third most commonly identified PIM, but in our study, only 12 patients were found to be using NSAIDs on a regular basis. The one reason for

this finding in our study is NSAIDs are commonly used in the community for a shorter period, but to be included in our study, there has to be a regular consumption of a drug for atleast 2 weeks. The risk factors associated with the use of renally inappropriate medication use were identified to be low socioeconomic status, use of OTC drugs, and reduced creatinine clearance. In a community based study done in the USA (37) , it was found that more than 50% of CKD patients who used OTC drugs were taking atleast one NSAID within a year. This portrays the magnitude of the problem. Even in our study we had significant proportions of patients with reduced creatinine clearance using or having used NSAIDs in the past (p=0.12).

9.4 Prevalence of ADEs:

One serious problem associated with inappropriate drug use is the increased risk of adverse drug events. Wu et al(38), studied the trends of hospitalisation due to ADR , over a period of 10 years, which showed an increasing trend of hospitalisation due to ADR with increasing in-hospital mortality. It has been shown that 80% of ADEs are dose related and only very few are allergic / idiosyncratic(39). Inappropriate drugs per se carry a higher risk for ADE. This was demonstrated by Albert et al(40), who showed a 1.8 to 1.9 times increased risk of hospitalization because of inappropriate drugs. The elderly population per se carry an independent risk for ADE by being a susceptible host, because of aging related physiological changes and increasing comorbid status increasing the drug – disease interactions resulting in serious outcomes.

Several studies reported that 10% - 15% of admissions in the elderly were because of drug related problems (41),(19),(42). In our study we identified that 71 patients (25%) had some form of drug related adverse event, of which 5 were purely because of drug omission , and

17 had presented to hospital with some other ailment and were identified to also have problems related to drug usage.

We attributed the increased number of Adverse Events mainly to high comorbid index (median of 6), increasingly aged population with mean age of 70 years and increased polypharmacy in our study population (53%).

Several studies have reported polypharmacy and higher co-morbid index was found to be independent risk factor for ADE(42), (43). In our study on univariate analysis, we identified people with higher co-morbid index (OR 2.01, p=0.132, CI 0.81 – 4.97) and use of polypharmacy (OR1.33, p=0.321, CI 0.76 – 2.32) as having an increasing trend in causing ADEs. However on multivariate analysis, this was not found to be statistically significant.

People with reduced creatinine clearance or CKD also had an increased risk for adverse effects (OR1.96, p=0.026, CI 1.08 – 3.56). But this was not significant on multivariate analysis. Kane –gill et al, in a retrospective study done in more than 1100 patients to assess the risk factors associated with ADEs, reported 16 times more risk for ADE in patients with reduced creatinine clearance.

On multivariate analysis, people with CAD, CVA and depression were at higher risk for developing ADE. The reason for patients with depression being more vulnerable to ADEs was due to concomitant use of various inappropriate drugs such as benzodiazepines (p=0.013), antidepressants with high anticholinergic activity (p<0.001) and even antipsychotics (p=0.002),all of which can precipitate delirium , produce falls and precipitate SAIO. Similarly, in patients with CAD, there is an increased risk for ADE, and this was mainly attributed to diuretic related hyponatremia, hypokalemia and ACEI & spironolactone related hyperkalemia. We could not find any studies in the literature analyzing the relationship of depression and CAD with the increased risk of ADE.

Similarly, patients who were completely dependent had an increasing trend towards developing ADEs, but this was not statistically significant. We could not find any statistical significant associations between age, cognitively impaired patient and occurrence of ADEs.

The most commonly offending drug class was identified to be the cardiovascular group of drugs (50.7%) which mainly includes diuretics (both loop and thiazide), ACEI & spironolactone. There were also a few cases of beta blocker related symptomatic bradycardia, dihydropyridine (CCB) related pedal oedema and alpha blocker related postural hypotension. This was followed by the CNS group of drugs (19.7%) mainly SIADH prone antidepressants, antipsychotics and anticonvulsants, delirium and fall related to benzodiazepines, and lastly drugs with anticholinergic activities precipitating delirium, SAIO and BOO. Mandavi et al (19), reported cardiovascular group of drugs to be the commonest offender in causing ADE in the Indian population.

In our study, more than fifty percent of events were related to dyselectrolytemias of which hyponatremia was the commonest, contributing 24% of the total adverse drug events. Davies et al(42) reported diuretics followed by anticoagulants as the commonest offender, which was consistent with our results. In our study, 6 ADEs was related to inappropriate anticoagulation resulting in significant morbidity to patients. In the ambulatory setting, the offending drugs may be totally different. In the study by Mandavi et al, pedal oedema related to dihydropyridines was the commonest ADEs. But in our study we had only 2 people on dihydropyridines developing pedal oedema.

One patient who presented with immune mediated CIDP with quadriparesis, developed respiratory depression to midazolam (2mg intravenous) given for procedural sedation resulting in death. Mandavi et all(19), reported the prevalence of severe ADE to be lesser

than 0.5%. No studies document any death related to ADE and there are only a few case reports of drug related mortality.

9.5 Prevalence of polypharmacy:

It has been shown in various studies that polypharmacy, is an important risk factor for PIM use and ADEs (11),(43),(44),(25),(19). In our study the mean ± SD number of drugs used per individual was 6 ± 4. The prevalence of people using more than 5 drugs (polypharmacy) was 53.9%, and of those using more than 10 drugs (excessive polypharmacy) was 15.7%. On univariate analysis, polypharmacy was found to have a significant association with PIM use and it showed an increasing trend for ADEs. But on multivariate analysis, polypharmacy did not have any significant association with PIM use or occurrence of ADEs.

Clinics in geriatrics, published an entire issue on polypharmacy, in May 2012, which quotes the following factors predisposing to use of polypharmacy,

1. Factors related to patients
    a) Age
    b) Gender
    c) Socioeconomic status
    d) Clinical conditions
2. Factors related to physicians
    a) Prescribing habits
    b) Medical guidelines
    c) The interaction between patient and physician

We have studied the above mentioned variables in our patients for assessing the correlation between these factors and polypharmacy use. On univariate analysis, we found that people

with high Charlson comorbidity index had a siginficant association with polypharmacy. With an index of more than 3, there is a 1.88 odds (p=0.091, CI0.90 – 3.90) of exposing to polypharmacy, which gets doubled if the index is > 6. (OR 4.55, p=<0.001, CI 2.15 – 9.62).

There is significant risk of polypharmacy seen with increasing age, dependency and worsening functional and cognitive status. Patients seeking more than 2 doctors were at greater risk (OR 4.35, p=<0.001, CI 2.11 – 8.97) for getting exposed to polypharmacy, and the main reason was found to be communication gap between doctors. On multivariate analysis, age, cognitive impairment and dependency status along with the presence of DM, CAD, CVA and depression were found to be independent risk factors for polypharmacy. Surprisingly, when adjusted, higher co-morbid index was not associated with polypharmacy. (OR 0.30, p=0.227, CI 0.04 – 2.09). The reason was attributed to the fact that higher proportions of people with diabetes mellitus and depression were present in the low comorbidity index group when compared to high index patients.

10. CONCLUSION

1. a) The prevalence of potentially inappropriate medication use in our study population was 33.2%.

   b) The majority of the population about 70% was found to be using one PIM and 21.3% were using two PIMs and very few, 7.5% were using more than 2 PIMs.

   c) The most common inappropriate drug class identified as benzodiazepines (19.5%), followed by conventional antimuscarinics (13.6%) and antipsychotics (11.9%).

   d) Age, functional status and depression were found to be independent risk factors for potentially inappropriate medication use.

The commonest drug – disease interaction found in our study was use of major and minor tranquilizers in the setting of falls, delirium and dementia, which constitutes 28.7%, followed by drugs with anticholinergic activity in patients with delirium, dementia, constipation and symptomatic LUTS, which constituted 21.9% of drug – disease interactions.

2. a) The prevalence of polypharmacy in our study group was 53.9%, and that of excessive polypharmacy was 15.7%. The average mean drug drug use per individual is 6.3.

   b) Age, cognitive impairment, dependency status and presence of diabetes mellitus and coronary artery disease were found to be independent risk factors for polypharmacy.

3. The prevalence of renally inappropriate drugs was found to be 5.7% in our study population. The most common renally inappropriate drug was identifies as non-steroidal anti-inflammatory drugs. On univariate analysis, people of low socio economic status, over the counter drug users and people with reduced creatinine

clearance (less than 60ml/min) were at increased risk for exposure to renally inappropriate drugs.

4. a) The prevalence of adverse drug effects resulting in hospitalisations was 25% in our study population.

   b) The most commonly offending drug class was cardiovascular drugs mainly diuretics, and the most common clinical presentation was found to be due to dyselectrolytemia, secondary to hyponatremia.

   c) Adverse drug events were associated with 0.14% in hospital mortality.

70% of the population had atleast one essential drug omitted according to start criteria. 4% of population had drug duplication. Our study population had a median comorbidity index of 6.

LIMITATIONS

Since the study was done in tertiary hospital, hence there is a potential for referral bias, and out patients also had a higher comorbid index or may not be a true representation of the community drug usage.

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13	837935f		3	67	3	1	1	0	0	1	probable CIDP	1	2	0	6	0.6	147.9	1.6	glynase 2.5 bd	eltroxin 25 od												0
14	851857f		1	60	2	1	1	0	0	0		1	2	1	6	1.2	70.1	3.8	glipizide 2.5 bd	telmisartan -	chlorthalidone 12.5 c	bisoprolol 2.5 od	ecosprin 75 od	eltroxin 50 od	pantop 40 od	livogen 1 od	shelcal 500 od	febuxostat 40 od	urimax d 1 od	mdi seroflo 250 bd		1
15	906323F		1	73	3	1	1	0	0	0		0		1	8	3.3	20.6	3.2	mixtard 8 - 0 - 8	stamlo 5 od	urimax 1 od	stator 10 hsod	eltroxin 75 od	mdi asthalin 100 prn								1
16	299488F		3	77	4	2	1	0	0	0		0	.a		9	2.9	17.9	3.4	MIXTARD 6 - 0- 6	CARVEDILOL	Tab.Isordil 10 mg thr	Tab.Sandocal 1 gr	Tab. Clopidogrel ;	Tab. Ecosprin 75 i	.Atorvastatin 10 r	Tabv. Pantoprazol	Tab. Febuxostat 4	Tab.calcit 0.25 mg o	ab.Autrin 1 tablet in	Tab.Folic acid 5 mg		1
17	974972B		3	68	3	2	1	0	0	0		1	2	.a	4	0.8	53.5	3.7	T.METFORMIN 1(	T.ECOSPIRIN	T.VIT B COMPLEX OD											0
18	634005f		1	58	2	1	1	0	0	0		1	3	1	7	1.6	45.4	4.6	Tab. Hydroxyurea	Tab. Folate 2	Tab. Dutas T 1 tablet	Tab. Febuxostat 4	Tab. Shelcal 500 mg once daily at night									0
19	858092F		3	75	4	1	1	0	0	0		0		0	4	0.7	80.4	4.6	t.amlo h od													0
20	506955f		1	71	3	2	5	0	0	0		1	3	.a	6	0.5	172.9	3.7	T. DYTOR 10mg O	T EPLERENO	ECOSPRIN 75 OD	LIVOGEN 1 OD	SHELCAL 500 OD	ELMECOB OD 500 OD								1
21	865136F		1	73	3	1	1	0	0	0		0		1	8	1.8	39.9	3.6	Inj.H.Mixtard 30/	nasal flutica	mdi formonide 400 c	mdi tiova 9 od	t theophylline 20	t montelukast 10	t fexofenadine 12	t bethanechol 25	t tamsulosin o.4 h	t eltroxin 100 od	t clinidipine 10 od	stator 10 hsod		1
22	513694d		1	59	2	2	1	0	0	0		0	.a		4	0.9	64.8	4.6	mdi seroflo 250 b	mdi asthalin	Inj. Lanctus 6 units s/	Tab. Metformin Si	Tab. Gliclazide MI	Tab. Sitagliptin 1(	Tab. Telmisartan ·	Tab. Amlodipine !	Tab. Minipres XL :	Tab. Deplatt-A 75mg	Tab. Stator 5mg onc	Tab. Pregabalin 75i		1
23	027178g		1	70	3	2	1	0	0	1	essential tremor	0	.a		7	0.8	74.2	3.8	metformin sr 1 , s	tamoxifen 2i	lorazepam 3 hsod	shelcal 500 od	pantop 40 od	stool laxative hso	ultracet prn								1
24	818067f		3	65	3	1	1	0	0	0		1	2	1	6	3.1	18	3.4	glyciphage 500 oc	glimepride 1	telmisartan h 40/12.!	urimax 1 od	h/o nitrofurantoin 100 bd x 7 days									0
25	549223d		2	64	2	2	1	0	0	0		1	3	.a	7	0.6	105.9	4.2	Tab Nitrofurtoin 1	Tab Amlodip	Tab Minipress XL 5m	Tab Ecosprin 75 i	Syp Lactulose 15r	Tab Pantop 40mg	tab methylocbalmine 1000 od								1
26	887211f		3	67	3	2	1	0	0	0		0	.a		2	0.7	84	3.9	cilacar 10 od	eltroxin 50 c	alprax 0.25 hsod	olanzapine 2.5 od	calcium 1 od									1
27	875130F		3	60	2	2	1	0	0	0		0	.a		2	1.1	49.9	3	t.eltroxin 50mg od													0
28		63523	2	80	4	1	1	0	0	0		0	.a		4	1	73.4	3.5														0
29	908008F		1	69	3	1	1	0	0	0		0		1	2	0.9	92.5	4.2	T.URIMAX 0.4 HS OD													0
30	847147B		1	75	4	1	1	0	0	0		1	2	1	6	1.8	37.4	3.6	Mycophenolate Si	Tablet Predr	Tablet shelcal 500mg	Tablet Pantoprazc	Tablet Amlodipin	Tablet Febuxostat	Tablet Aspirin 75	Tablet Atorvastati	Tablet Mecobalan	Tablet Folic Acid 5 Mg once a day					1
31	310348C		3	70	3	1	1	0	0	0		1	1	0	4	0.8	99.3	3.1	T.DYTOR 5 MG BI	T.CLOPIDOG	T.RAMIPRIL 2.5 MG h	T.DIGOXIN 0.25 6 DAYS A WEEK										0
32	092861C		2	58	2	2	1	0	0	0		0	.a		1	0.7	84.5	2.7	MDI ASTHALIN 100 PRN													0
33	711758D		1	52	1	1	1	0	0	0		0		1	4	1	88.6	4.8	T.ZOLPIDEM 10M	T.MULTIVITA	T.DERIPYLINE R 150 MG BD												0
34	846662F			60	2	2	1	0	0	0		0		0	3	0.7	104.9	4.1	T.PANTOP 40 MD	T.TELMISARTAN 40 MG HS OD													0
35	894208F		3	61	2	1	1	0	0	0		0		0	3	0.6	102.9	4.3	tramadol prn													0
36	876759F		3	64	2	1	1	0	0	0		0		0	3	0.9	80.1		T.AMLOKIND AT 5/50 OD													0
37	400236F		3	65	3	1	1	0	0	0		0		0	3	1.2	64.5	3.2	MDI.FORMIDE 20(	MDI.TIOVA !	MDI.ASTHALIN 100 P	T.DERIPHYLINE SR 150 BD										0
38	874158F		3	64	2	2	1	0	0	0		0	.a		4	0.6	91.1	3.7	INJ.GLAGINE 6 Uh	T.METAPROI	T.ATORVASTATIN 5 MG HS OD												0
39	072583A		1	77	4	2	1	0	0	0		0	.a		6	0.7	103.5	3.5	T.Glyciphage 1 gn	T.Deplatt 75	T.Shelcal 500mg od	T.Glimepride 1 m	T.pantop 40 mg o	T.Doxofyline 400	MDI sero flow 25	MDI Asthalin 100 mi	PRN					1
40	755695F		1	73	3	1	1	0	0	0		1	2	0	5	2.6	25.1	3.3	T.Paracetamol 1 g	mdi ASTHAL	TAB ANTHTN DETAIL!	EMPRICALL 4 DRUG ATT --> DIHI										0
41	83999Of		3	61	2	1	1	0	0	0		1	3	0	4	1.1	64.5	4.2	T.Neurobion od	T.Donepezil 5 mg od													0
42	908734F		1	84	4	2	1	0	0	0		1	2	.a	6	0.8	66.7	3.7	T.Lasix 20 mg od	T.Carvedelol	T.Ramipril 5 mg od	T.Angispan TR 2.5	T.Deplatt 75 /150	T.Atarvastatin 20	T.Doxophyline 40(	T.Pantop 40 mg o	T.Domstal 10 mg	T.Livogen od	T.Shelcal 500 mg od	T.Mirtazapine 7.5 i		1
43	019550G		1	68	3	1	1	0	0	0		1	1	1	5	0.9	95.5	3.9	T.Metaprolol XL 2	T.Telmisarta	T.Syncapone 100 tid	T.TRimetazidine M	T.Ranolozine500 i	T.Deplatt A75/15(	T.Atarvastatin 10	T.Dutas T od	T.Folate 5 mg od	T.Pantop 40 mg od	T.Shelcal od			1

44	773292A		1	80	4	2	1	0	0	0	1	1	.a		7	0.8	71	4.4 T.Glyciphage 1gm T.Gliclazide ı T.sitagliptin 100 mcg T.Losartan 25 mg T.Dytor 10 mg od T.Dilzem SR 90 r T.Ecosprin 75 m T.Rosuvastatin 1(T.Lorazepam 2 mg hs od	1
45	713355A		2	81	4	2	1	0	0	0	0		.a		8	1.3	45.2	4.1 Inj.Actrapid 22-0- Inj.Insulitard T.Atenolol 50 mg od T.Clinidepine 5 m T.Atarvostatin 10 .Sandocal od T.Ecospirin75 mg T.Gliclazide 80 mg T.Osteophos 70 r T.Minipress XL 5 mg Naturolax powder 2 T.Pantop 40mg on	1
46	835901D		1	83	4	2	1	0	0	0	0		.a		11	0.5	109.7	2.9 T.Metformin 500 Tab. Stator 1 Tab. Aspirin 75 Mg 1 Tab. Shelcal 1 tab t.Livogen od T.Pregabalin 75 T.Resperidone 0 naturolax powder t amlodipine 5 od	1
47	769363C		1	72	3	2	1	0	0	1 Bells palsy 54 yrs b	0		.a		3	0.9	60.2	3.8 T.Bisoprolol 2.5 m T.Amlodepin T.Tonact 10 mg hs c T.Ecospirin 75 mg od	0
48	893116F		1	67	3	1	1	0	0	0	0			1	4	1	81.7	T.Glipizide 5 mg T.Metformin T.sitagliptin 50 mg T.Atarvastatin 10 mg od	0
49	327236C		1	49	1	1	1	0	0	0	0			0	3	0.7	138.5	3.9 Tab. Pregabalin 7 Tab Olmesa Tab. Sitagliptin 100m Tab. Metformin SI Tab. Ecosprin 75r Tab. Thiamine 10 Tab. Folate 5mgs Tab. Methylcobal T.Alprox 0.25 mg Tab. Sandocal 500m Tab. Prothiadin 50 n Tab. Pantoprazole	1
50	035695G		3	70	3	2	1	0	0	1 subaracnoid cyst	0		.a		3	1.2	68.8	3.9 T.Domperidone 1 Tablet Amlo Tablet Olmesartan 2(T.Pantop 40 mg od	0
51	673824D		3	67	3	1	1	0	0	1 BOO 2* to MSA	0			0	6	1.3	62.1	3.5 C.Amantadine hyc T.Amlo 2.5 mg od	0
52	834190F		3	80	4	2	1	1	0	1 LL Sensory neurop	1	2	.a		8	1.2	40.7	3.9 T.Telmisartan 40 mg od	0
53	864438A		3	67	3	2	1	0	0	0	0		.a		4	0.7	88.9	4.6 T.Pantop 40 mg (T.Lisino pril T.Metformin SR 1gm T.Atorvastatin 1(T.Ecospirin 75 mg od	0
54	510659F		3	79	4	2	1	0	0	0	0		.a		4	0.5	84	T.Metformin SR 1 T.Glibenclan T.Sandocal 500 mg T.Neurobion forb T.Amilene 10 mg hs od	0
55	003642G		3	60	2	2	1	0	0	0	0		.a		4	0.6	92.5	2.8 T.Telma AM 40/5 T.Pantop 40 T.Itopride 50 mg o T.Sandocal od T.MVT od	0
56	005242G		3	75	4	1	1	0	0	0	0			0	6	1.4	60.6	3.6 T.Syndopa 275 1 T.Pacitane 2 tid	0
57	873574F		3	60	2	1	1	0	0	1 NPH	0			1	7	1.6	43.8	3.7 T.Losartan 50mg T.Amlo 5 m T.Syndopa 110 Qid T.Sodium valproa T.Ropinirole XL 2 T.Piracetam 200 T.Clopidogrel 75 mg od	1
58	009457G		3	62	2	1	1	0	0	0	1	2		0	4	5.6	10	2.4 T.Envas 5 mg oc T.Amlo 5 mg od	0
59	895725D		3	69	3	1	1	0	0	0	0			1	7	0.8	90.2	3.8 T.Metformin 500 T.Glimepirid T.Aspirin 75 mg od T.Urimax od T.Atarvostatin 10 mg od	0
60	012516G		3	70	3	2	1	1	0	0	1	2	.a		6	8.6	3.3	3.8 NSAIDS injections every monthly	0
61	839189B		3	74	3	1	1	0	0	0	0			1	5	0.8	97.7	T.Metformin SR T.Daonil 5 ı T.Nicardia R 20 mg T.Envas 2.5 mg T.Ecospirin 75 m T.Atarvastatin 10 mg hs od	1
62	892687F		3	66	3	1	1	0	0	0	1	2		0	11	0.5	129.4	2.7 T.Pantop 40 mg od	0
63	445588F		3	64	2	1	1	0	0	0	1	2		1	11	2	30.5	2 T.Pantop 40 mg (T.Serutan 2 T.Antoxid od T.NEurobion forte T.Livogen bd T>clopidogrel 15 T.Sandocal od T.Pregabalin 75 ı Inj.Actrapid 8-7-4 Inj.Insulitard 0-0-4	1
64	000338G		3	68	3	1	1	0	0	1 ?b12 related neurc	1	2		1	3	1	76	4.1 T.Envas 2.5 mg ı T.Angispan MR 2.5 mg od	0
65	008019G		3	63	2	1	1	0	1	0	0			1	3	0.8	71.7	4.2 T.Haloperidol 0.2! T.Clonazepa T.Amlo 5 mg od Syrp.Rantac Mps ı Pow.ISAPGOL hus T.Pacitane 2 mg bd	1
66	917373F		2	74	3	2	1	0	0	1 critical illness polyn	1		.a		10	0.8	79.7	2.3 T.carvedilol 6.5 n T.Amiodaror T.Atarvastatin 20 mg T.Warfarin 5 mg T.Dytor 10 mg od	0
67	683875D		3	73	3	1	1	0	0	0	0			1	8	1.2	62.8	3.2 Tab Glimepride 1ı Tab Pantopr Tab Envas 2.5mg onc Tab Dutas-T once Tab Ecosprin 75m Tab Deriphyllin retard 150 mg twice dail	1
68	616771C		3	77	4	2	1	0	0	0	0		.a		6	0.7	82.4	3.4 T.Alendronate 70 t shelcal 50(Calcirol GRANULES NSAIDS prn	0
69	834834f		3	85	5	1	1	0	0	0	0			0	7	1	68.1	4 T.Donepezil 5 mg T.Quetiapine Calcigard 20 mg bd T.Atenolol 50 mg AM od	0
70	899470D		3	68	3	2	1	0	0	0	1	2	.a		8	2	29.4	T.Deplatt 75/150 T.Glimepirid T.Pantop 40 mg od T.Clacar 10 mg ı T.Metoprolol XL 5 T.Autor 10 mg h T.Dytor 10-0-5mg	1
71	025386g		3	58	2	1	1	0	0	0	0			0	5	0.6	167.9	2.2 T.Ecospirin 75 mj T.Atarvastati DM DIET	0
72	032146G		3	85	5	2	1	0	0	0	1	2	.a		5	1.2	42.2	2.7 T.Pantop 40 mg o T.Sandocal ! METACIN PRN	0
73	767239F		3	66	3	2	1	0	0	1 MITOCHONDRIAL E	0		.a		8	0.6	91.5	3.4 T.Lithium 400 mg T.Olanzapine T.Amitryiline 25 mg T.Clobazam 1mg T.Lesuride 25 mg T.Esntalopran 20 T.Lorazepam 0.5 ı T.Valproate 500 n T.Neostigmine 7.5 T.Donepezil 5 mg hs inj solumedrol250 ti inj fosphenytoin 3(	1
74	393499C		3	66	3	1	1	0	0	0	1	1		0	7	0.9	77.5	T.Nicrondil 5 mg T.Vildagliptin T.Deplatt A od T.Atarvostatin 20 T.Amitryptyline 1(T.Trimetazidine M T.Cardace 1.25 r T.Amlo 5 mg od T.Prednisolone 2.5 mg od	1
75	269559f		3	65	3	2	1	0	0	0	1	2	.a		7	2.6	25.2	T.Dytor 10 mg od T.Trimetazid T.Angispan TR 2.5 m T.Deplatt A 75 mj T.Atarvastatin 10 T.Pantop 40 mg (T.Livogen od T.Sandocal 500 m mixtard 23-0-24	0
76	606694F		1	73	3	1	1	0	0	0	0			1	7	1.3	56.5	3.5 Tab. Mycophenol Tab Clopidog Tab Amlodipine 5mg Tab Stator 10mg (Tab Alendronate ! Tab Septran DS 1 Tab Shelcal 500 n Tab Pantoprazole Tab Clonazepam (Tab Urimax 0.4 mgs T.Valporate 300 mg T.Metformin 500	1
77	953155D		2	61	2	2	1	0	0	0	0		.a		9	3.6	15.7	3.3 Inj Actrapid 32 Inj Insulotari Tab. Atenolol 50mg t Tab. Nicardia Ret Tab. Clonidine 10 Tab. Minipress XL Tab. Clopidogrel ! Tab. Stator 10mg Tab. Livogen 1 tw Tab. Shelcal 500mg ı Tab. Sevalamer 400 Tab. Pantoprazole	1
78	344138A		2	60	2	2	1	1	0	0	0		.a		5	0.9	65.6	3.5 Inj. Actrapid 28-0 Inj.NPH 24 ı T.Metformin SR 1gn T.Gliclazide 40 m T.Amlo 5 mg od T.Envas 10 mg b T Aspirin 75 mg T.Atarvastatin 10 T.Shelcal od T.Metacin 1 gm prn	1
79	854431f		3	65	3	2	1	0	0	0	0		.a		4	2.9	15.6	4 NSAIDS regular use	0
80	000126G		2	66	3	2	1	0	0	0	0		.a		7	1	61.3	3.8 Inj.H.Mixtard 12 (Tab. Metfori Tab. Glipizide 5mg tv Tab. Losartan 50r Tab. Ecosprin 75i Tab. Stator 10mg Tab. Eltroxin 50m Tab. Pantoprazole Tab. Shelcal 500m Tab. Alendronate 70 T.Becosels od T.Pregabalin 75 mg	1
81		854371	3	68	3	1	1	0	0	0	0			1	6	1.4	54.9	3.7 Inj Human Mixtar Tab Gliclazic Tab ecosprin 75 mg (Tab Atorvastatin ! T.Minipress XL 5 T.Rantac 150 mg stamlo 10 mg od	1
82							.a	.a	.a	.a			.a						.a
83	462027A		2	56	2	2	1	1	0	0	1	2	.a		5	0.6	113	3.3 T.MTX 25 mg 1/7 T.Folic acid T.Sazo 1. 5g bd T.Sandocal 500m T.Eltroxin 100 mc T.Rabeprazole 20 T.Itopride 50 mg l Naturolax 2tsp hs od	1
84	021008G		3	60	2	2	1	0	0	1 depression	0		.a		2	1	57.3	4.4 Tab Clonazepam (T.Thyroxine T.Escilatilopram 10 n T.Amylene 12.5 m T.Chlordiazepoxid T.Pantop 40 mg o Syrup.cremaffin 20 ml hs od	1
85	891146F		3	65	3	1	1	0	0	0	0			1	2	0.6	137.6	1.8 T.Ursodeoxycholi T.Prednosoli Ayurvedic medicine v ?Anti HTN	0
86	474643F		1	61	2	2	1	0	0	0	1	2	.a		10	0.9	66.1	3.7 Tab. Mycophenol Tab. Predni Tab. Shelcal 500mg t Inj.Actrapid 22-0- INJ. Insulatard ; Tab. Metformin S Tab. Nifedipine-R Tab. Deplatt-A 75 Tab. Stator 10 mg Tab. Eltroxin 125mcg T.Pantop 40 mg od T.Udiliv 450-0-300	1
87	794719C		2	80	4	1	1	0	0	0	0			1	9	1.1	74.1	4.1 T. Metformin SR 1 T. Glipizide ; T. Shelcal 500mg onc T. Pantoprazole 4 T. Pregabalin 75 T. Clopidogrel 75 T. Atorvastatin 1(T.Losartan 50 mg T.Ismo 20 mg bd T.Ca gluconate 325 ı T.Urimax od T.Sotalol 40 mg bd	1
88	846262D		3	67	3	2	1	0	0	0	0		.a		5	0.7	92.8	4.3 T.Metformin SR ! T.Pantop 40 Naturolax	0

89	415986D	3	69	3	1	1	0	0	0	0		0	6	0.8	93.9	3.3	Tab Syndopa 100,	Tab Amlodip	Tab Aspirin 75mg on	Tab Atorvastatin :	Tab Pregabalin 75	t.chrono 500 mg	T.Glipizide 2.5 mg	T.Metoprolol XL 2	T.Tolterodine 2 m	T.Pantop 40 mg od	Syrup.Cremafin		1
90	808520F	3	71	3	2	1	0	0	0	0	.a		7	5.5	9.6	3.3	Tab. Pantoprazole	Tab. Sandoc	Tab. Nifedipine retar	Tab. Metoprolol x	Tab. Minipress XL	Tab. Livogen one	INj.Cyclophospha	T.Prednisolone 4	T.Septran ss od	T.Folate 5 mg 5/7			1
91	866567B	3	69	3	2	1	0	0	0	1	2 .a		9	1.5	45.7	4.1	Inj Actrapid 15 - (	Inj NPH 1	Tab Losartan 50mg t	Tab Atorvastatin :	Tab Doxophylline	Tab Pantoprazole	Tab Clindipine 5n	Tab Bisoprolol 5n	Tab Metformin 5(	Tab Glimipride 1mg	Tab Clopidogrel 75n	Tab Trimetazidine (	1
92	021908G	3	83	4	1	1	0	0	0	0		1	7	1.2	66.2	3.7	LIquid parafin prr	MDI Asthalir	DM diet										0
93	009090F	3	78	3	1	1	0	0	0	0		1	4	1.1	66.6	3.3	T.metformin SR 1	T.Glipizide 1	T.Envas 5 mg od	T.Deplatt Aod	T.Atarvastatin 10 mg hs od								0
94	020098G	3	72	3	1	1	0	0	0	0		1	5	1.3	65.8	4	T.Ecospirin 150 o	T.Prasugrel :	T.Stator 10 hs od	T.Dytor 10 mg od	T.Losartan 50 od								0
95	021466G	3	60	2	1	1	0	0	0	0	.a		4	0.7	111	4	Tab. Metformin S	Tab. Glimep	T.Aten 50 mg 0d	T.Telmisartan 40	T.Hydrochiorotiaz	T.Pantop 40 mg o	T.Tonact 10 mg h	T.Clonazepam 0.5	T.Vertin 24 mg bc	T.Tyroxine 50mcg o(	T.Lorazepam 1 mg l	T.Triflupenrazine+t	1
96	038376G	3	59	2	1	1	0	0	0	1	2	1	9	3.5	18	4	Inj.Mixtard 8-0-8	T.Pantop 40	T.Aspirin 75 mg od	T.Levetiracetam 2	T.Livogen od								0
97	028860G	1	76	4	1	2	0	0	0	1	1	1	7	1.2	73.3	3.3	T.Metformin SR 5	T.Gliclazide	T.Sitagliptin 100 mg (	T.Amlo 10 mg od	T.Nicrandil 5 mg l	T.Cilostazol 100 n	T.Pentoxiphyline (	T.Ecospirin 75 mg	T.Atarvastetin 10	T.urimax 0.4 mg od	Syrup.Cremafin	Inj.Mix 16-0-10	1
98	011821G	3	69	3	1	1	0	0	0	1	2	0	5	4.9	12.5	3.9	T.Amlo 5 mg bd												0
99	004528G	3	61	2	1	1	0	1	1 dysthymia	0		1	4	1.3	71.3	4.2	Inj.Mixtard 30/70	T.Pantop 40	T.ramipril 2.5 mg od	T.Met XL 25 mg A	T.Esintalopram 1(	T.Clonazepan 0.5	T.Tramadol prn	T.Cinarizine					1
100																													
101																													
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exces	in1	in1a	in1b	in1b1	in1c	in1c1	in1d	in1d1	in1e	in1e1	in1f	in1f1	in1f2	in1g	in2	in2a	in2a1	in2a2	in2a3	in2a4	in2a5	in3a	in3a1	in3b	in3b1	in3c	
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		1	0	.a		.a			0		0		1		4	13	1	2		2				0		0	0
	0	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	0	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		1	0	.a		.a			0		0		0			11	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	0	1	0	.a		.a			0		0		0			11	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	1	1	0	.a		.a			0		0		0			9	0							0		0	0
	0	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	1	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	0	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
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	1	0	.a	.a		.a		.a		.a			0			13	0							0		1	0
	0	0	.a	.a		.a		.a		.a			0			13	1	2		1	2			0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	0	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	0	1	0	.a		.a			0		0		1			4	1	2		1	1			0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	0	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	1	2		1			2	0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	0	0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
.a		0	.a	.a		.a		.a		.a			0			13	0							0		0	0
	1	1	0	.a		.a			0		0		0			9	0							0		0	0
	1	0	.a	.a		.a		.a		.a			0			13	0							0		0	0

	0	0 .a	.a		.a		.a		.a			0			13	1	1	1	2			0		0			0
	1	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	0	1	0 .a		.a			0		0		1		4	13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	1	1	0 .a		.a			0		1		0			13	1	2	1	1			0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		1	0 .a		.a			0		1	1	0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		1	1	1	1	0		0		0		0			13	0						0		0			0
	0	0 .a	.a		.a		.a		.a		.a					0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	0	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	0	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	0	1	1	1	1	0		1		0		1	3		11	1	2	2		2		0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	0	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			1	3		13	0						0		0			0
.a		1	0 .a		.a			0		0		1		3	13	0						0		0			0
	0	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	1	1	1	1	1	0		0		1	1	1			4	1	2	1	2		2	0		0			0
	0	1	0 .a		.a			0		1	1	0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	1	0 .a	.a		.a		.a		.a			0			13	1	2	2		2		0		0			0
	1	0 .a	.a		.a		.a		.a			0			13	0						0		1	1		1
	0	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	1	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	0	0	1 .a		.a		.a		.a			0			13	0						0		0			0
.a	.a	.a	.a		.a		.a		.a		.a				.a						.a		.a		.a		
	0	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	0	1	0 .a		.a			0		1	1 .a				6	1	2	2		2		0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	1	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
	1	0 .a	.a		.a		.a		.a			0			13	0						0		0			0
.a		0 .a	.a		.a		.a		.a			0			13	0						0		0			0

1	1	0	.a	.a		0	0	0		1	0					0	0	0
0	0	.a	.a	.a		.a	.a	0		13	0					0	0	0
1	0	.a	.a	.a		.a	.a	0		13	0					0	0	0
.a	0	.a	.a	.a		.a	.a	0		13	0					0	0	0
.a	0	.a	.a	.a		.a	.a	0		13	0					0	0	0
.a	0	.a	.a	.a		.a	.a	0		13	0					1	0	0
1	1	1	1	1	0	0	0	1	5	13	1	2	1	2	2	0	0	0
.a	0	.a	.a	.a		.a	.a	0		13	0					0	0	0
1	0	.a	.a	.a		.a	.a	0		13	0					0	0	0
.a	0	.a	.a	.a		.a	.a	0		13	0					0	0	0
0	1	0	.a	.a		1	1	0		6	1	2	2		2	0	0	0

in3c1	in3d	in3e	in3f	in3f1	in3g	in4a	in4b	in4c	in4d	in4d1	in4e	in4f	in5a	in5a1	in5a2	in5b	in5b1	in5c	in5d	in5e	in5f	in3	in1a1	in1b2	in1c2	in1d2	in1e2	in4
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	1	2	0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		1	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	1
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		1	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0
	0	0	0		0	0	0	0	0		0	0	0	0		0		0	0	0	0	0	.a	.a	.a	.a	.a	0

0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	.a	.a	.a	.a	.a	1
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0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	.a	.a	.a	.a	.a	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	.a	.a	.a	.a	.a	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	.a	.a	.a	.a	.a	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	.a	.a	.a	.a	.a	0

in2a6	in2b	in2c	in2d	in2d1	in2d2	in5	in3a2	in3b2	in3c2	in3d1	in3e1	in3f2	in3g1	in6	in4a1	in4b1	in4c1	in4d2	in4e1	in4f1	in4g	in4f2	in4g1	in7	in5a3	in5b2	in5c1	in5d1
.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a	.a	.a	.a		1	0	0	0	0	0	0	0	0	0	0 .a	.a	.a	.a
.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a
.a	.a	.a	.a	.a	.a		1	0	0	0	0	0	0	0	0 .a	.a	.a	.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a
.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a
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.a		1	0	0	0	0	0	0	0 .a	.a	.a	.a		1	0	0	1	0	0	0	0	0	0 .a		0 .a	.a		0 .a		0 .a	.a
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.a	1	0	0	0	0	0	0	0 .a	.a	.a	.a		0 .a	.a		0 .a	.a	.a	.a	.a		1	0	0 .a	.a	0 .a		0 .a	.a	
.a	1	0	0	0	0	0	0	0 .a	.a	.a	.a		1	0	0	1	0	0	0	0	0	0 .a		0 .a	.a	1	0	1	0	0
.a	0 .a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a		0 .a	.a		0 .a	.a	.a	.a	.a		0 .a		0 .a	.a	1	0	0 .a	.a	
.a	0 .a	.a	.a	.a	.a	.a		1	0	0	0 .a		0 .a	.a		1	0	0	0	0	0	0 .a		0 .a	.a	1	0	0 .a	.a	
.a	1	0	1	1	0	0	0	1	0	0	0	0	0 .a	.a		1	1	0	0	0	1	0 .a		0 .a	.a	0 .a		0 .a	.a	
.a	1	0	0	0	0	0	0	1	0	0	0	0	0 .a	.a		1	0	0	0	0	0	0 .a		0 .a	.a	1	0	0 .a	.a	
.a	1	0	0	0	0	0	0	0 .a	.a	.a	.a		0 .a	.a		1	0	0	0	0	0	0 .a		0 .a	.a	1	0	0 .a	.a	
.a	0 .a	.a	.a	.a	.a	.a		0 .a	.a	.a	.a		0 .a	.a		0 .a	.a	.a	.a	.a		0 .a		0 .a	.a	0 .a		0 .a	.a	
.a	0 .a	.a	.a	.a	.a	.a		1	0	0	0	0	0 .a	.a		1	0	0	1	1	0	0 .a		0 .a	.a	1	1	0 .a	.a	

in16	in2a7	in2a8	in2a9	in2a10	in2a11	in2a12	in2a13	in2a14	in2a15	in2a16	in17	in3a3	in1a3	in1a4	in18	in19	in20	in21	in22	in23	in24	in25	in26	in27	in28	in29	in30	in31	in1a5	in1a6	in1b4
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	1	0	0	0	1	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	1		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0										0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		1	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	0											0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	1	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	1	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	0											0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		1	0	0	0	1	1	0	0	0	0	0	0	0	1	1	0
	1	0	0	0	0	0	0	0	0	0	0	1	0	0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	1	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	0											0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	0											0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	1	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		
	1	0	0	0	0	0	0	0	0	0	0	0		0		0	0	0	0			0	0	0	0	0	0	0	0		

1	0	0	1	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	1	0	0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	1	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	1	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0	1	0	0	0	0	0	0	0	0	0 .a		.a	
1	1	1	0	0	1	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	1	0	0	0	0	0	0	0	0 .a		1	5	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0		0
1	0	0	0	0	0	0	0	0	0	0	1	0	0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		1		0	0	0	0	1	0	0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0 .a		.a	
1	1	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	1	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	1 .a		0		0	0	0	0	1	1	0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0	0	0	0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0		0
1	0	0	0	0	0	0	0	0	0	0	0 .a		1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0		0
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0	0	0	0	1	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	
1	0	0	0	0	0	0	0	0	0	0	0 .a		0		0	0	0	0 .a	.a		0	0	0	0	0	0	0	0 .a		.a	

in1c3	in1d3	in1e3	in1f3	in1g1	in1h	in1i	in1j	in1k	in1l	in1m	in1n	in32	numb	outcome	
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	0	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	4	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		1	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		1	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	3	2
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1
	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		1	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		1	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		1	3	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	3	1
	0	0	0	1	0	0	0	0	0	0	0	0	1	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		1	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		1	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	2
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	2	1
	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	1
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	1	2
.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a		0	4	1

.a .a .a .a .a .a .a .a .a .a .a .a 0 4 1

.a .a .a .a .a .a .a .a .a .a .a .a 1 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 3 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 4 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 1 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 1 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 1 2 1

0 0 0 0 0 0 0 0 0 0 0 0 1 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

0 0 0 0 0 0 0 0 0 0 0 0 1 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 1 1

0 0 0 0 0 0 0 0 0 0 0 0 1 3 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 3 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 1 1

0 0 0 0 0 0 0 0 0 0 0 0 1 3 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 1 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 4 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

0 0 0 0 0 0 0 0 0 0 0 0 1 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 1 1 1

0 0 0 0 0 0 0 0 0 0 0 0 1 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 1 1

0 0 0 0 0 0 0 0 0 0 0 0 1 1 1

.a .a .a .a .a .a .a .a .a .a .a .a 0 2 1

.a .a .a .a .a .a .a .a .a .a .a .a 1 1 1

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Annexures

1 – BEER'S INDEX

2 – START CRITERIA

3 – DATA ABSTRACTION FORMS

4 – KUPPUSWAMY – MODOFOED SOCIOECONOMIC STATUS ASSESSMENT SCALE

5 - BARTHEL INDEX

6 – TIMED GET UP TEST

7 – MINI COG ASSESSMENT

8 – GDS ASSESSMENT

9 – CONSENT FORMS

1 - BEER'S CRITERIA

Organ System or Therapeutic Category or Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Anticholinergics (excludes TCAs)				
First-generation antihistamines (as single agent or as part of combination products) Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Dexchlorpheniramine Diphenhydramine (oral) Doxylamine Hydroxyzine Promethazine Triprolidine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; greater risk of confusion, dry mouth, constipation, and other anticholinergic effects and toxicity. Use of diphenhydramine in special situations such as acute treatment of severe allergic reaction may be appropriate	Avoid	Hydroxyzine and promethazine: high; All others: moderate	Strong
Antiparkinson agents Benztropine (oral) Trihexyphenidyl	Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more-effective agents available for treatment of Parkinson disease	Avoid	Moderate	Strong
Antispasmodics Belladonna alkaloids Clidinium-chlordiazepoxide Dicyclomine Hyoscyamine Propantheline Scopolamine	Highly anticholinergic, uncertain effectiveness	Avoid except in short-term palliative care to decrease oral secretions	Moderate	Strong
Antithrombotics				
Dipyridamole, oral short acting* (does not apply to extended-release combination with aspirin)	May cause orthostatic hypotension; more-effective alternatives available; intravenous form acceptable for use in cardiac stress testing	Avoid	Moderate	Strong
Ticlopidine*	Safer effective alternatives available	Avoid	Moderate	Strong
Anti-infective				
Nitrofurantoin	Potential for pulmonary toxicity; safer alternatives available; lack of efficacy in patients with CrCl < 60 mL/min due to inadequate drug concentration in the urine	Avoid for long-term suppression; avoid in patients with CrCl < 60 mL/min	Moderate	Strong
Cardiovascular				
$Alpha_1$ blockers Doxazosin Prazosin Terazosin	High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile	Avoid use as an antihypertensive	Moderate	Strong
Alpha agonists, central Clonidine Guanabenz* Guanfacine* Methyldopa* Reserpine (> 0.1 mg/d)*	High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension	Avoid clonidine as a first-line antihypertensive. Avoid others as listed	Low	Strong

Organ System or Therapeutic Category or Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Barbiturates Amobarbital* Butabarbital* Butalbital Mephobarbital* Pentobarbital* Phenobarbital Secobarbital*	High rate of physical dependence; tolerance to sleep benefits; risk of overdose at low dosages	Avoid	High	Strong
Benzodiazepines *Short and intermediate acting:* Alprazolam Estazolam Lorazepam Oxazepam Temazepam Triazolam *Long acting:* Clorazepate Chlordiazepoxide Chlordiazepoxide-amitriptyline Clidinium-chlordiazepoxide Clonazepam Diazepam Flurazepam Quazepam	Older adults have increased sensitivity to benzodiazepines and slower metabolism of long-acting agents. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, periprocedural anesthesia, end-of-life care	Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium	High	Strong
Chloral hydrate*	Tolerance occurs within 10 days, and risks outweigh benefits in light of overdose with doses only 3 times the recommended dose	Avoid	Low	Strong
Meprobamate	High rate of physical dependence; very sedating	Avoid	Moderate	Strong
Nonbenzodiazepine hypnotics Eszopiclone Zolpidem Zaleplon	Benzodiazepine-receptor agonists that have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); minimal improvement in sleep latency and duration	Avoid chronic use (> 90 days)	Moderate	Strong
Ergot mesylates* Isoxsuprine*	Lack of efficacy	Avoid	High	Strong
Endocrine				
Androgens Methyltestosterone* Testosterone	Potential for cardiac problems and contraindicated in men with prostate cancer	Avoid unless indicated for moderate to severe hypogonadism	Moderate	Weak
Desiccated thyroid	Concerns about cardiac effects; safer alternatives available	Avoid	Low	Strong
Estrogens with or without progestins	Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women Evidence that vaginal estrogens for treatment of vaginal dryness is safe and effective in women with breast cancer, especially at dosages of estradiol < 25 μg twice weekly	Avoid oral and topical patch. Topical vaginal cream: acceptable to use low-dose intravaginal estrogen for the management of dyspareunia, lower urinary tract infections, and other vaginal symptoms	Oral and patch: high Topical: moderate	Oral and patch: strong Topical: weak
Growth hormone	Effect on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose	Avoid, except as hormone replacement after pituitary gland removal	High	Strong

Organ System or Therapeutic Category or Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Antiarrhythmic drugs (Class Ia, Ic, III) Amiodarone Dofetilide Dronedarone Flecainide Ibutilide Procainamide Propafenone Quinidine Sotalol	Data suggest that rate control yields better balance of benefits and harms than rhythm control for most older adults. Amiodarone is associated with multiple toxicities, including thyroid disease, pulmonary disorders, and QT- interval prolongation	Avoid antiarrhythmic drugs as first-line treatment of atrial fibrillation	High	Strong
Disopyramide*	Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred	Avoid	Low	Strong
Dronedarone	Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or heart failure. In general, rate control is preferred over rhythm control for atrial fibrillation	Avoid in patients with permanent atrial fibrillation or heart failure	Moderate	Strong
Digoxin > 0.125 mg/d	In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity; slow renal clearance may lead to risk of toxic effects	Avoid	Moderate	Strong
Nifedipine, immediate release*	Potential for hypotension; risk of precipitating myocardial ischemia	Avoid	High	Strong
Spironolactone > 25 mg/d	In heart failure, the risk of hyperkalemia is higher in older adults especially if taking > 25 mg/d or taking concomitant NSAID, angiotensin converting-enzyme inhibitor, angiotensin receptor blocker, or potassium supplement	Avoid in patients with heart failure or with a CrCl < 30 mL/min	Moderate	Strong
Central nervous system				
Tertiary TCAs, alone or in combination: Amitriptyline Chlordiazepoxide-amitriptyline Clomipramine Doxepin > 6 mg/d Imipramine Perphenazine-amitriptyline Trimipramine	Highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low-dose doxepin ($\leq$6 mg/d) is comparable with that of placebo	Avoid	High	Strong
Antipsychotics, first (conventional) and second (atypical) generation (see Table 8 for full list)	Increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia	Avoid use for behavioral problems of dementia unless nonpharmacological options have failed and patient is threat to self or others	Moderate	Strong
Thioridazine Mesoridazine	Highly anticholinergic and risk of QT-interval prolongation	Avoid	Moderate	Strong

Organ System or Therapeutic Category or Drug	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Insulin, sliding scale	Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting	Avoid	Moderate	Strong
Megestrol	Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults	Avoid	Moderate	Strong
Sulfonylureas, long duration Chlorpropamide Glyburide	Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes syndrome of inappropriate antidiuretic hormone secretion. Glyburide: greater risk of severe prolonged hypoglycemia in older adults	Avoid	High	Strong
Gastrointestinal				
Metoclopramide	Can cause extrapyramidal effects including tardive dyskinesia; risk may be even greater in frail older adults	Avoid, unless for gastroparesis	Moderate	Strong
Mineral oil, oral	Potential for aspiration and adverse effects; safer alternatives available	Avoid	Moderate	Strong
Trimethobenzamide	One of the least effective antiemetic drugs; can cause extrapyramidal adverse effects	Avoid	Moderate	Strong
Pain				
Meperidine	Not an effective oral analgesic in dosages commonly used; may cause neurotoxicity; safer alternatives available	Avoid	High	Strong
Non–COX-selective NSAIDs, oral Aspirin > 325 mg/d Diclofenac Diflunisal Etodolac Fenoprofen Ibuprofen Ketoprofen Meclofenamate Mefenamic acid Meloxicam Nabumetone Naproxen Oxaprozin Piroxicam Sulindac Tolmetin	Increases risk of GI bleeding and peptic ulcer disease in high-risk groups, including those aged > 75 or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. Use of proton pump inhibitor or misoprostol reduces but does not eliminate risk. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months and in approximately 2–4% of patients treated for 1 year. These trends continue with longer duration of use	Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent (proton pump inhibitor or misoprostol)	Moderate	Strong
Indomethacin Ketorolac, includes parenteral	Increases risk of GI bleeding and peptic ulcer disease in high-risk groups. (See above Non-COX selective NSAIDs.) Of all the NSAIDs, indomethacin has most adverse effects	Avoid	Indomethacin: moderate Ketorolac: high	Strong
Pentazocine*	Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs; is also a mixed agonist and antagonist; safer alternatives available	Avoid	Low	Strong
Skeletal muscle relaxants Carisoprodol Chlorzoxazone Cyclobenzaprine Metaxalone Methocarbamol Orphenadrine	Most muscle relaxants are poorly tolerated by older adults because of anticholinergic adverse effects, sedation, risk of fracture; effectiveness at dosages tolerated by older adults is questionable	Avoid	Moderate	Strong

2 – START/STOP CRITERIA

Table 5. Potential prescribing omissions identified by the START criteria	
CRITERIA	
A Cardiovascular system	
1 y 2 Warfarin (Acenocumarol) or Aspirin in the presence of chronic atrial fibrillation (AF).	7
5 Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy is >5years.	6
6 Angiotensin converting enzyme (ACE) inhibitor with chronic heart failure.	3
B Respiratory system	
1 Regular inhaled beta 2 agonist or anticholinergic agent for mild to moderate asthma or chronic obstructive pulmonary disease (COPD).	7
C Central nervous system	
1 L-DOPA in idiopathic Parkinson's disease with definite functional impairment and resultant disability.	1
2 Antidepressant drug in the presence of moderate–severe depressive symptoms lasting at least 3 months.	5
D Gastrointestinal system	
1 Proton pump inhibitor with severe gastro-oesophageal acid reflux disease	1
2 Fibre supplement for chronic, symptomatic diverticular disease with constipation.	2
E Musculoskeletal system	
3 Calcium and Vitamin D supplement in patients with known osteoporosis.	12
F Endocrine system	
1 Metformin with Type 2 diabetes (in the absence of renal impairment*).	3
3 Antiplatelet therapy in diabetes mellitus with co-existing major cardiovascular risk factors (hypertension, hypercholesterolaemia, smoking history).	3
4 Statin therapy in diabetes mellitus if co-existing major cardiovascular risk factors present.	8
TOTAL Potential prescribing omissions	58
*Serum creatinine >150 mmol l-1, or estimated GFR 20–50 ml min-1.	

Table 4. Potential inappropriate medicines identified by the STOPP criteria.	
CRITERIA	
A Cardiovascular system	
3 Loop diuretic as first-line monotherapy for hypertension.	4
8 Calcium channel blockers with chronic constipation.	3
12 Aspirin at dose >150 mg day.	6
13 Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event.	5
B Central nervous system and psychotropic drugs	
7 Long-term (i.e., >1 month), long-acting benzodiazepines and benzodiazepines with long-acting metabolites, e.g. diazepam.	7
8 Long-term (i.e,. >1 month) neuroleptics as long-term hypnotics.	14
9 Long-term neuroleptics (>1 month) in those with parkinsonism.	1
D Respiratory system	
3 Nebulized ipratropium with glaucoma.	1
E Musculoskeletal system	
2 NSAID with moderate–severe hypertension.	6
3 NSAID with heart failure.	2
4 Long-term use of NSAID (>3 months) for symptom relief of mild osteoarthritis.	4
6 NSAID with chronic renal failure*.	1
G Endocrine system	
1 Glibenclamide or chlorpropamide with Type 2 diabetes mellitus.	3
H Drugs that adversely affect fallers	
1 Benzodiazepines.	5
2 Neuroleptic drugs.	1
J Duplicate drug classes	
Any duplicate drug class prescription (two concurrent: NSAIDs, benzodiazepines)	3
TOTAL	66
*Serum creatinine >150 mmol l^{-1}, or estimated GFR 20–50 ml min^{-1}.	

3 - DATA ABSTRACTION FORM

Serial number

PATIENT INFORMATION

Patient's name: .....
Hospital no: .....

Age: Sex: M(1) / F (2)

Marital status: Married(1) / Single(2) / Others - separated(3) / widow(4) / divorced(5)

Address for communication:

SOCIO – ECONOMIC STATUS:

Education: ..... < 5^{th} std (1) / 6^{th} – 12^{th} (2) / diploma (3) / master degree (4)

Occupation: .....

Income: ..... < 3000/month (1) / 3000 – 10,000(2) / 10,000 – 50,000 (3) / > 50,000 (4)

Govt pension / insurance benefits

Living with: alone / husband / children / informal care giver / others

According to revised Kuppusamy scale 2012

I	Upper class	25-29
II	Upper middle class	16-25
III	Lower middle class	11-15
IV	Upper lower class	5-10
V	Lower class	<5

PERFORMANCE STATUS :

ADL - dependent / independent

Barthrel index: .....

Timed get up and go test: .....

(Freely mobility <10 sec / Variable mobility 10-20 sec / Impaired mobility >20 sec)

Vision RE ..... LE .....

Hearing (whispering test) RE ..... LE .....

Cognitive status - Any problem with memory: Yes/No

If yes, Mini Cog: .....

Depressed - yes or no

If yes, Geriatric Depression Scale (5 item short version) .....

MEDICAL STATUS:

List of Co morbid conditions:

No	Co morbid condition	Duration	Details
1			
2			
3			
4			
5			
6			
7			

Charlson co morbidity index: .....

Screening for other diseases:

No	Diseases	Status	
1	Heart failure	Present (1)	Absent (2)
2	CKD	Present (1)	Absent (2)
3	Epilepsy	Present (1)	Absent (2)
4	Dementia	Present (1)	Absent (2)
5	Parkinson's disease	Present (1)	Absent (2)
6	h/o GI bleed	Present (1)	Absent (2)
7	h/o syncope	Present (1)	Absent (2)
8	h/o delirium	Present (1)	Absent (2)
9	h/o falls & fractures	Present (1)	Absent (2)
10	Constipation	Present (1)	Absent (2)
11	LUTS	Present (1)	Absent (2)
12	Urinary incontinence	Present (1)	Absent (2)

PHARMACOKINETIC FACTORS

Problems with swallowing - Yes/No

h/o GI surgery/CLD/alcoholism

BMI: ..... (Under weight <18.50 / Normal 18.50-24.99 / Overweight >25)

Creatinine..... CrCl (ml/min/1.73m^2) .....

Stage I CrCl > 90

Stage II CrCl 60-89
Stage III CrCl 30-59
Stage IV CrCl 15-29
Stage V CrCl <15 or req dialysis

LFT: .....

DRUG DETAILS :

NO.	DRUG	DRUG CLASS	DOSAGE & TIMINGS	INDICATION FOR USE
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				

15				

Treated by physician / geriatrician /others

Number of attending doctors: .....

Is there any proper communications between doctors or record accessibility - Yes/No

Frequency of health check up: .....

Cost for monthly drugs: .....

Self medication use - Yes /No

OTC medication use - Yes /No

Patient's understanding of their drugs:

Compliance ..... concordance .....

Self administration of drugs / given by care giver

ADVERSE DRUG EVENTS :

Drug causing ADR with dosage _____

Is it inappropriate or not: Yes/No

Is it renally appropriate or not: Yes/No

H/O hospitalisation because of ADR - Yes/No

How many days of in hospital stay_____

ICU care required or not – Yes/No

Cost of the hospital stay_____

4 - REVISED KUPPUSAMY SOCIO ECONOMIC STATUS SCALE

Revised table (Table 1) for scales in 2012 to define socioeconomic status thus obtained is as follows.

Table: 1. Kuppuswamy's Socioeconomic Status Scale

(A) Education Score		
1	Profession or Honours	*7*
2	Graduate or post graduate	*6*
3	Intermediate or post high school diploma	*5*
4	High school certificate	*4*
5	Middle school certificate	*3*
6	Primary school certificate	*2*
7	Illiterate	*1*

(B) Occupation Score		
1	Profession	*10*
2	Semi-Profession	*6*
3	Clerical, Shop-owner, Farmer	*5*
4	Skilled worker	*4*
5	Semi-skilled worker	*3*
6	Unskilled worker	*2*
7	Unemployed	*1*

(C) Monthly family income in Rs		*Score*	*Modified for 1998* [3] *in* Rs	Modified for 2012 in Rs
1	≥ 2000	*12*	≥ 13500	≥32050
2	1000-1999	*10*	6750 - 13499	*16020 – 32049*
3	750-999	*6*	5050 - 6749	*12020 – 16019*
4	500-749	*4*	3375 - 5049	*8010 – 12019*
5	300-499	*3*	2025 - 3374	*4810 – 8009*
6	101-299	*2*	676 - 2024	*1601 – 4809*
7	≤ 100	*1*	≤ 675	*≤ 1600*

Total Score	Socioeconomic class
26-29	Upper (I)
16-25	Upper Middle (II)
11-15	Middle/Lower middle (III)
5-10	Lower/Upper lower (IV)
<5	Lower (V)

5 -BARTHEL INDEX

Bowels
0 = incontinent (or needs to be given enemata)
1 = occasional accident (once/week)
2 = continent
Patient's Score: _____

Bladder
0 = incontinent, or catheterized and unable to manage
1 = occasional accident (max. once per 24 hours)
2 = continent (for over 7 days)
Patient's Score: _____

Grooming
0 = needs help with personal care
1 = independent face/hair/teeth/shaving (implements provided)
Patient's Score: _____

Toilet use
0 = dependent
1 = needs some help, but can do something alone
2 = independent (on and off, dressing, wiping)
Patient's Score: _____

Feeding
0 = unable
1 = needs help cutting, spreading butter, etc.
2 = independent (food provided within reach)
Patient's Score: _____

Transfer
0 = unable – no sitting balance
1 = major help (one or two people, physical), can sit
2 = minor help (verbal or physical)
3 = independent
Patient's Score: _____

Mobility
0 = immobile
1 = wheelchair independent, including corners, etc.
2 = walks with help of one person (verbal or physical)
3 = independent (but may use any aid, e.g., stick)
Patient's Score: _____

Dressing
0 = dependent
1 = needs help, but can do about half unaided
2 = independent (including buttons, zips, laces, etc.)
Patient's Score: _____

Stairs
0 = unable
1 = needs help (verbal, physical, carrying aid)
2 = independent up and down
Patient's Score: _____

Bathing
0 = dependent
1 = independent (or in shower)
Patient's Score: _____

Total Score: _____

6 – TIMED GET UP AND GO TEST

Instructions:

The person may wear their usual footwear and can use any assistive device they normally use.

1. Have the person sit in the chair with their back to the chair and their arms resting on the arm rests.
2. Ask the person to stand up from a standard chair and walk a distance of 10 ft. (3m).
3. Have the person turn around, walk back to the chair and sit down again.

Timing begins when the person starts to rise from the chair and ends when he or she returns to the chair and sits down.

The person should be given 1 practice trial and then 3actual trial. The times from the three actual trials are averaged.

Predictive Results

Seconds	**Rating**
<10	Freely mobile
<20	Mostly independent
20-29	Variable mobility
>20	Impaired mobility

Source: Podsiadlo, D., Richardson, S. The timed 'Up and Go' Test: a Test of Basic Functional Mobility for Frail Elderly Persons. *Journal of American Geriatric Society*. 1991; 39:142-148

7 - MINI COG TEST

Mini-Cog test is a 3-minute instrument to screen for cognitive impairment in older adults in the primary care setting. The Mini-Cog uses a three-item recall test for memory and a simply scored clock-drawing test (CDT). The latter serves as an “informative distractor,” helping to clarify scores when the memories recall score is intermediate.

SCORING

1 point for each recalled word

Score clock drawing as **Normal** (the patient places the correct time and the clock appears grossly normal) or **Abnormal**

Score

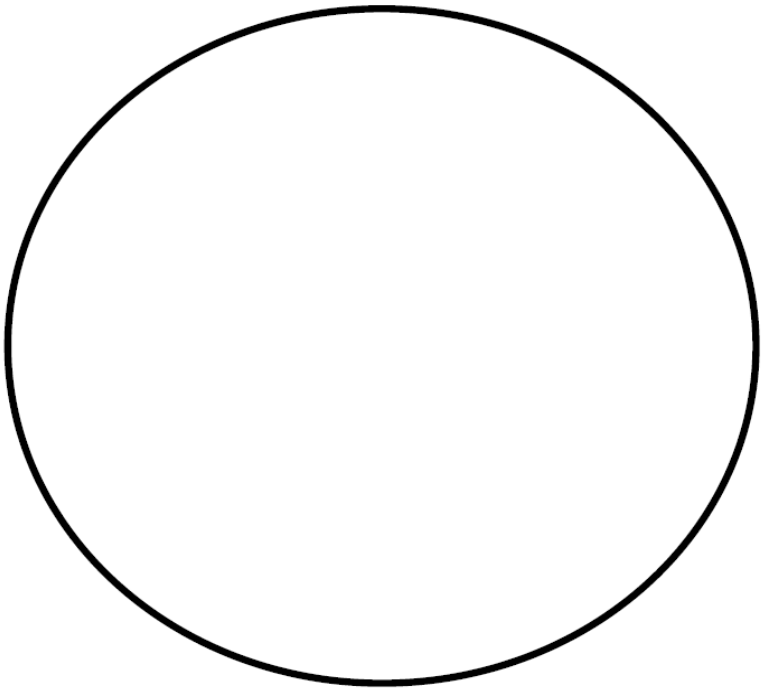
0	Positive for cognitive impairment
1-2	**Abnormal** CDT then positive for cognitive impairment
1-2	**Normal** CDT then negative for cognitive impairment
3	Negative screen for dementia (no need to score CDT)

INSTRUCTIONS:
0
1. Instruct the patient to listen carefully and repeat the following :

APPLE WATCH PENNY
PEN PENCIL PAPER

2. Administer the Clock Drawing Test

(Inside the circle draws the hours of a clock as if a child would draw them
Place the hands of the clock to represent the time “forty five minutes past ten o’clock”)



3.Ask the patient to repeat the word given previously

Scoring

Number of correct items recalled _____ [if 3 then negative screen. STOP]

If answer is 1-2
Is CDT Abnormal? No Yes

If No, then negative screen
If Yes, then screen positive for cognitive impairment

8 - GERIATRIC DEPRESSION SCALE

Geriatric Depression Scale five item shorter version

Please read the following questions.

To each question answer YES or NO.

Are you basically satisfied with your life?

Do you often get bored?

Do you often feel helpless?

Do you prefer to stay at home rather than going out and doing new things?

Do you feel pretty worthless the way you are now?

‘No' in Q1 and 'yes' in Q2-5 score 1

Total score of 2 is positive.

(Rinaldi P, Mecocci P, Benedetti C, Ercolani S, Bregnocchi M, Menculini G, et al. Validation of the five-item geriatric depression scale in elderly subjects in three different settings. Journal of the American Geriatrics Society. 2003; 51(5):694-98)

9- CHARLSTON COMORBIDITY INDEX

Table 1. Charlson Comorbidity Index Scoring System

Score	Condition
1	Myocardial infarction (history, not ECG changes only)
	Congestive heart failure
	Peripheral vascular disease (includes aortic aneurysm ≥6 cm)
	Cerebrovascular disease: CVA with mild or no residua or TIA
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Peptic ulcer disease
	Mild liver disease (without portal hypertension, includes chronic hepatitis)
	Diabetes without end-organ damage (excludes diet-controlled alone)
2	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes)
	Tumor without metastases (exclude if >5 y from diagnosis)
	Leukemia (acute or chronic)
	Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor
	AIDS (not just HIV positive)

NOTE. For each decade > 40 years of age, a score of 1 is added to the above score.

10 - PATIENT CONSENT FORMS

POTENTIALLY INAPPROPIATE MEDICATION USE IN HOSPITALIZED ELDERLY

Patient information sheet:

Inappropriate medication use is common in elderly and it is associated with adverse health outcomes. Avoiding the use of inappropriate and high-risk drugs is an important, simple, and effective strategy to reduce medication-related problems in older adults. The study that you are requested to take part in will estimate the magnitude of inappropriate medication use in our elderly population and analyse the risk factors associated with it.

Participating in the study is entirely voluntary and you can decide to withdraw from the study at any point in time. This will not affect the treatment you will be undergoing in this hospital.

What will I have to do to take part in the part?

i. Sign the consent form
ii. Give demographic details
iii. Give a detailed history – including drug history

Is there any risk?

There is no risk to the patients involved in this study.

Will I have to pay for investigations?

Patients will not be charged for this study.

What advantage will I get from this study?

a) By participating in this study, the patient is aware of the consequences of inappropriate drug usage.
b) The patients will have a rational drug prescription by discharge,

Will my personal details be kept confidential?

We aim to publish the results of this study in a medical journal, but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission.

Can I withdraw from this study after it starts?

Participation in this study is entirely voluntary; you can withdraw from the study at any time. Refusal to participate will not involve any loss of benefits to which you are otherwise entitled.

If you have any further questions, please ask Dr. Alwin Thilak
You can contact me on
Phone 04162282943 / 9994029782
Email: alwyn1612@gmail.com

Informed Consent form to participate in a research study

Study Title: POTENTIALLY INAPPROPIATE MEDICATION USE IN ELDERLY

Study Number: _____

Subject's Initials: _____

Subject's Name: _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: Dr.Alwin Thilak Christopher. J

Signature of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____